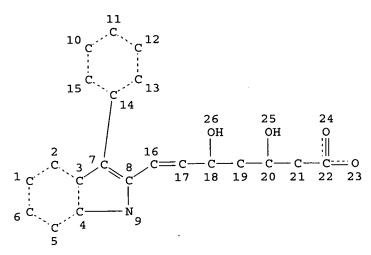
=> d 15 que stat;fil caplus;s 15
L1 STR



NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE L3 STR

Ca 1

NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 1

STEREO ATTRIBUTES: NONE

L5 2 SEA FILE=REGISTRY SSS FUL L1 AND L3

100.0% PROCESSED 2 ITERATIONS 2 ANSWERS SEARCH TIME: 00.00.01

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
162.62
162.83

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FILE COVERS 1907 - 1 Sep 2005 VOL 143 ISS 10 FILE LAST UPDATED: 31 Aug 2005 (20050831/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

3 L5 L6

=> d 1-3 ibib abs hitstr

ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:182623 CAPLUS

DOCUMENT NUMBER: 142:280050

Novel process for preparation of 7-[3-(4-fluorophenyl)-TITLE:

1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-6-

heptenoic acid sodium salt

INVENTOR(S): Srinath, Sumithra; Puthiaparampil, Tom Thomas; Ganesh,

Sambasivam

PATENT ASSIGNEE(S): Biocon Limited, India SOURCE: PCT Int. Appl., 14 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| P | PATENT NO. | | | | KIN | D | DATE | | | | | | | DATE | | | |
|---|------------|------|------|------|------|------|------|------|------|------|------|--------|------|------|------|------|----------|
| W | 0 2005 | | | | A1 | _ | 2005 | 0303 | | | | | | | 2 | 0030 | 826 |
| | W: | ΑE, | AG, | AL, | AM, | ΑT, | AU, | AZ, | BA, | BB, | BG, | BR, | BY, | BZ, | CA, | CH, | CN, |
| | | | | | | | DK, | | | | | | | | | | |
| | | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | KE, | KG, | KP, | KR, | KZ, | LC, | LK, | LR, |
| | | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | ΜZ, | NI, | NO, | NZ, | OM, |
| | | PG, | PH, | PL, | PT, | RO, | RU, | SD, | SE, | SG, | SK, | SL, | SY, | ΤJ, | TM, | TN, | TR, |
| | | TT, | TZ, | UA, | UG, | US, | UZ, | VN, | YU, | ZA, | ZM, | ZW | | | | | |
| | RW: | GH, | GM, | KΕ, | LS, | MW, | MZ, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, | ΑZ, | BY, |
| | | KG, | ΚZ, | MD, | RU, | ТJ, | TM, | ΑT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | EE, | ES, |
| | | FI, | FR, | GB, | GR, | HU, | ΙE, | IT, | LŲ, | MC, | NL, | PT, | RO, | SE, | SI, | SK, | TR, |
| | | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML, | MR, | NE, | SN, | TD, | TG |
| PRIORI' | TY APP | LN. | INFO | . : | | | | | | WO 2 | 003- | IN28 | 7 | | 2 | 0030 | 826 |
| OTHER : | SOURCE | (S): | | | CAS | REAC | T 14 | 2:28 | 0050 | | | | | | | | |
| AB A | proce | ss f | or t | he p | repa | rati | on o | f (3 | R,5S | ,6E) | -7-[| 3 - (4 | -flu | orop | heny | 1)-1 | -(1- |
| methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-6-heptenoic acid (I) sodium | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | lution c |
| I or its salt with a suitable cation to afford an insol. salt I, (b) | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | |

A f isolation of the insol. salt of I, (c) conversion of the insol. salt of I

to I sodium salt. This process is economic since expensive reactants/reagents are not employed. It is simple since it involves salt formation at ambient conditions. Also it is a highly efficient purification method, as only salt of required product ppts. All impurities which do not form salt with second cation remain in the solution, thus resulting in isolation of the product with a high degree of purity. No further purification of the product is required and hence the number of steps is reduced. It results in high yields as no byproducts are formed and recovery of insol. salt is almost quant. It also results in high isomeric purity of the product, as it avoids lactonization and saponification, during which epimerization

may occur. Thus, to a solution of [(4R,6S)-6-[(1E)-2-[3-(4-fluorophenyl)-1-isopropyl-1H-indol-2-yl]vinyl]-2,2-dimethyl-[1,3]dioxan-4-yl]acetic acid tert-Bu ester (2.5 g, 0.005 mol) in MeCN (40 mL), aqueous HCl (7.5 mL, 0.1 N) was added and stirred for 2 h at 30-35°. After cooling the reaction mixture to room temperature, aqueous sodium hydroxide (10 mL, 10%) was added

and stirred for 16 h at room temperature. The reaction mixture was concentrated under

reduced pressure and water (30 mL) was added to the residue. The solution was further concentrated (25 mL volume) and extracted with Me tert-Bu ether (2 \times 15

mL). After adjusting the pH of aqueous layer to 7.0-7.2 by adding aqueous HCl (1.0 N), a solution of calcium acetate (0.6 g, 0.0038 mol) in water (10 mL) was added under stirring at $20-22^{\circ}$. The reaction mixture was further stirred for 30 min to completely precipitate calcium salt of fluvastatin. It

filtered and dried to give pure fluvastatin calcium salt which was suspended in water (15 mL) and pH of the mixture was adjusted to 4.0-5.0 by adding aqueous HCl (1.5 N). The aqueous layer was extracted with ether (2 x 15 mL),

combined ether extract was washed with brine and concentrated. The residue was mixed with water (15 mL) and a solution of sodium hydroxide (0.14 g, 0.035 mol) in water (1 mL) was added. After stirring for 15 min, the reaction mixture was washed with ether (2 x 15 mL). The aqueous layer was freeze-dried to get pure fluvastatin sodium salt.

IT 634902-71-9P

was

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; novel process for preparation of 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-6-heptenoic acid sodium salt via precipitation of insol. salt and its conversion to sodium salt)

RN 634902-71-9 CAPLUS CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

●1/2 Ca

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:1006762 CAPLUS

DOCUMENT NUMBER: 140:47480

TITLE: Calcium salts of indole derived statins

INVENTOR(S): Chen, Guang-Pei; Kapa, Prasad Koteswara; Sutton, Paul

Allen

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PAT | PATENT NO. | | | | KIND DATE | | | APPLICATION NO. | | | | | DATE | | | | |
|----------|------------|------|------|-----|-----------|-----|------|-----------------|-----|------|-------|-------|------|-----|-------------|------|-----|
| | | | | | | - | | | | | | | | | | | |
| WO | 2003 | 1058 | 37 | | A1 | | 2003 | 1224 | Ţ | WO 2 | 003-1 | EP61. | 95 | | 20 | 0030 | 512 |
| | W: | ΑE, | AG, | ΑL, | AM, | ΑT, | AU, | ΑZ, | BA, | BB, | BG, | BR, | BY, | ΒZ, | CA, | CH, | CN, |
| | | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | ES, | FI, | GB, | GD, | GE, | GH, |
| | | HR, | HU, | ID, | IL, | IN, | ıs, | JP, | KE, | KG, | ΚP, | KR, | KZ, | LC, | LK, | LT, | LU, |
| | | LV, | MA, | MD, | MK, | MN, | MX, | NΙ, | NO, | NZ, | OM, | PH, | PL, | PT, | RO, | RU, | SC, |
| | | SE, | SG, | SK, | ТJ, | TM, | TN, | TR, | TT, | UA, | US, | UZ, | VC, | VN, | YU, | ZA, | zw |
| | RW: | AM, | ΑZ, | BY, | KG, | ΚZ, | MD, | RU, | ТJ, | TM, | ΑT, | BE, | BG, | CH, | CY, | CZ, | DE, |
| | | DK, | EE, | ES, | FI, | FR, | GB, | GR, | HU, | ΙE, | IT, | LU, | MC, | NL, | PT, | RO, | SE, |
| | | SI, | SK, | TR | | | | | | | | | | | | | |
| CA | 2486 | 557 | | | AA | | 2003 | 1224 | (| CA 2 | 003-: | 2486 | 557 | | 2 | 0030 | 512 |
| EP | 1515 | 717 | | | A1 | | 2005 | 0323 |] | EP 2 | 003- | 7402 | 34 | | 2 | 0030 | 512 |
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| | | ΙE, | SI, | LT, | LV, | FΙ, | RO, | MK, | CY, | ΑL, | TR, | BG, | CZ, | EE, | ΗU, | SK | |
| PRIORITY | Y APP | LN. | INFO | .: | | | | | 1 | US 2 | 002- | 3883 | 18P | j | 2 (| 0020 | 513 |
| | | | | | | | | | | WO 2 | 003-1 | EP61 | 95 | 7 | v 20 | 0030 | 512 |
| | | | | | | | | | | | | | | | | | |

OTHER SOURCE(S): MARPAT 140:47480

AB The present invention provides calcium salts of indole-derived statins.

More specifically, the invention provides fluvastatin calcium (I), in a highly crystalline form. Furthermore, the present invention is directed to methods for the preparation of I, and to pharmaceutical compns. comprising the crystalline form. The I is effective for the prevention and/or treatment of hypercholesterolemia, hyperlipoproteinemia, dyslipidemia, and atherosclerosis.

IT 634902-71-9P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of crystalline fluvastatin Ca salt and blood

cholesterol-lowering

effects thereof)

RN 634902-71-9 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

●1/2 Ca

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

3

ACCESSION NUMBER:

2003:154436 CAPLUS

DOCUMENT NUMBER:

INVENTOR(S):

138:204870

TITLE:

Processes for preparing calcium salt forms of statins Niddam-Hildesheim, Valerie; Lifshitz-Liron, Revital;

Lidor-Hadas, Rami

PATENT ASSIGNEE(S):

Teva Pharmaceutical Industries Ltd., Israel; Teva

Pharmaceuticals USA, Inc.

SOURCE:

PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO. | KIND DAT | TE AI | PPLICATION NO. | DATE |
|---------------|---------------|--------------|-------------------|-----------------|
| | | | | |
| WO 2003016317 | A1 200 | 030227 WC | O 2002-US26012 | 20020816 |
| W: AE, AG, A | L, AM, AT, AU | U, AZ, BA, E | BB, BG, BR, BY, I | BZ, CA, CH, CN, |
| CO, CR, C | J, CZ, DE, DI | K, DM, DZ, B | EC, EE, ES, FI, G | GB, GD, GE, GH, |
| GM, HR, H | J, ID, IL, IN | N, IS, JP, H | KE, KG, KP, KR, 1 | KZ, LC, LK, LR, |
| LS, LT, L | J, LV, MA, MI | D, MG, MK, N | MN, MW, MX, MZ, 1 | NO, NZ, OM, PH, |
| PL, PT, R | D, RU, SD, SE | E, SG, SI, S | SK, SL, TJ, TM, 1 | IN, TR, TT, TZ, |
| UA, UG, U | S, UZ, VC, VI | N, YU, ZA, 2 | ZM, ZW, AM, AZ, 1 | BY, KG, KZ, MD, |
| RU, TJ, T | 1 | | | |
| RW: GH, GM, K | E, LS, MW, M2 | Z, SD, SL, S | SZ, TZ, UG, ZM, S | ZW, AT, BE, BG, |
| CH, CY, C | Z, DE, DK, E | E, ES, FI, F | FR, GB, GR, IE, 3 | IT, LU, MC, NL, |
| PT, SE, S | (, TR, BF, B) | J, CF, CG, C | CI, CM, GA, GN, | GQ, GW, ML, MR, |
| NE, SN, T |), TG | | | |

| 5 - | _ | | | | | | | | | | | | | | | | | |
|-------|------|------|------|------|-----|-----|--------|-------|-----|----|-------|------|-------|-----|----|------|-----|-----|
| | US | 2002 | 0992 | 24 | | A1 | 200 | 20725 | U | S | 2001- | 3741 | 2 | | | 200 | 110 | 24 |
| | US | 6528 | 661 | | | B2 | 200 | 30304 | | | | | | | | | | |
| | CA | 2450 | 820 | | | AA | 200 | 30227 | C | Ά | 2002- | 2450 | 820 | | | 200 | 208 | 16 |
| | US | 2003 | 1146 | 85 | | A1 | 200 | 30619 | U | S | 2002- | 2225 | 56 | | | 200 | 208 | 16 |
| | US | 6777 | 552 | | | В2 | 200 | 40817 | | | | | | | | | | |
| | ΕP | 1425 | 287 | | | A1 | 200 | 40609 | E | P | 2002- | 7593 | 74 | | | 200 | 208 | 16 |
| | | R: | AT, | BE, | CH, | DE, | DK, ES | , FR, | GB, | GR | , IT, | LI, | LU, | NL, | SE | E, M | C, | PT, |
| | | | IE, | SI, | LT, | LV, | FI, RO | , MK, | CY, | AL | , TR, | BG, | CZ, | EE, | SI | ζ . | | |
| | TR | 2003 | 0228 | 1 | | T2 | 200 | 40921 | T | 'R | 2003- | 2003 | 02283 | l | | 200 | 208 | 16 |
| | CN | 1543 | 468 | | | Α | 200 | 41103 | C | 'N | 2002- | 8159 | 99 | | | 200 | 208 | 16 |
| | JP | 2005 | 5003 | 82 | | T2 | 200 | 50106 | J | P | 2003- | 5212 | 39 | | | 200 | 208 | 16 |
| | | 5299 | | | | | | 50324 | N | Z | 2002- | 5299 | 13 | | | 200 | 208 | 16 |
| | ZA | 2003 | 0093 | 73 | | Α | 200 | 41202 | Z | Ά | 2003- | 9373 | | | | 200 | 312 | 02 |
| | NO | 2004 | 0010 | 82 | | Α | 200 | 40315 | N | O | 2004- | 1082 | | | | 200 | 403 | 15 |
| | US | 2004 | 1766 | 15 | | A1 | 200 | 40909 | U | S | 2004- | 8034 | 14 | | | 200 | 403 | 18 |
| PRIOF | YTIS | APP | LN. | INFO | . : | | | | U | S | 2001- | 3128 | 12P | | P | 200 | 108 | 16 |
| | | | | | | | | | U | S | 2001- | 3741 | 2 | | A | 200 | 110 | 24 |
| | | | | | | | | | U | IS | 2000- | 2493 | 19P | | P | 200 | 011 | .16 |
| | | | | | | | | | U | IS | 2001- | 3121 | 44P | | P | 200 | 108 | 13 |
| | | | | | | | | | U | S | 2001- | 3265 | 29P | | P | 200 | 110 | 01 |
| | | | | | | | | | U | S | 2002- | 2225 | 56 | | Α3 | 200 | 208 | 16 |
| | | | | | | | | | W | Ю | 2002- | US26 | 012 | | W | 200 | 208 | 16 |
| | | | | | | | | | | | | | | | | | | |

OTHER SOURCE(S): MARPAT 138:204870

Page 6

AΒ Processes for preparing hemicalcium salts of a statins RCH(OH)CH2CH(OH)CH2CO2H (R = statin organic radical selected from pravastatin, fluvastatin, cerivastatin, atorvastatin, rosuvastatin, pitavastatin, simvastatin, or lovastatin) from an ester derivative or protected ester derivative of the statin by using calcium hydroxide are provided. The ester or protected ester derivative is contacted with calcium hydroxide to obtain the calcium salt. Preferred statins are rosuvastatin, pitavastatin and atorvastatin, simvastatin and lovastatin. In processes beginning with a protected satin ester derivative, the protecting group is hydrolyzed during salt formation by contact with calcium hydroxide, or is contacted with an acid catalyst followed by contact with calcium hydroxide. Thus, diol-protected atorvastatin ester I (R = CMe3, R3R5 = CMe2) was treated with an 80% aqueous soln of AcOH at rt for 20 h to form the deprotected ester I (R = CMe3, R3 = R5 = H) which was in turn dissolved in EtOH, treated with a saturated soln of Ca(OH)2 containing Bu4N+Br- and stirred at

45° for 24 h to give atorvastatin hemicalcium salt I (R = 1/2Ca, R3

= R5 = H) in 77% yield for the two steps.

IT 500103-16-2P, Fluvastatin hemicalcium

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(processes for preparing calcium salt forms of statins)

RN 500103-16-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, calcium salt (2:1), (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-). Double bond geometry as shown.

●1/2 Ca

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> => d l14 que stat;d l15 que stat;fil caplus;s l14 and l5 L10 STR

3

NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

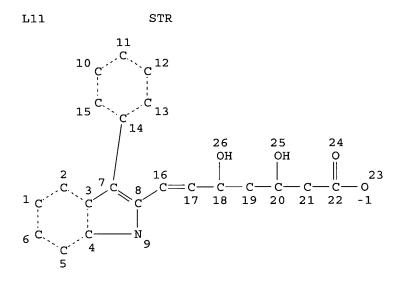
GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 27

STEREO ATTRIBUTES: NONE

113 SEA FILE=REGISTRY SSS FUL L10

100.0% PROCESSED 215 ITERATIONS 113 ANSWERS

SEARCH TIME: 00.00.01



NODE ATTRIBUTES:

CHARGE IS E-1 AT 23 DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE

L15 O SEA FILE=REGISTRY SSS FUL L11

100.0% PROCESSED 403 ITERATIONS 0 ANSWERS

SEARCH TIME: 00.00.01

| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
|--|------------|---------|
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 483.99 | 824.32 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -2.19 |

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FILE COVERS 1907 - 1 Sep 2005 VOL 143 ISS 10 FILE LAST UPDATED: 31 Aug 2005 (20050831/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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1 L14 AND L5 L16

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L16 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:1006762 CAPLUS

DOCUMENT NUMBER: 140:47480

TITLE: Calcium salts of indole derived statins

INVENTOR (S): Chen, Guang-Pei; Kapa, Prasad Koteswara; Sutton, Paul

Novartis A.-G., Switz.; Novartis Pharma G.m.b.H. PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT | PATENT NO. | | | | KIND DATE | | | APPLICATION NO. | | | | | DATE | | | |
|--------------|------------|------|-----|-----|-----------|-------|------|-----------------|-------|-------|-------|-----|------|------|-------|-----|
| | 21250 | | | | - | | 1004 | | | | | · | | | | |
| WO 200 | 31028 | 3 / | | AΙ | | 2003. | 1224 | , | WO 2 | 003-1 | ELQT: | 95 | | 20 | 00306 | 512 |
| W: | ΑE, | AG, | AL, | AM, | AΤ, | AU, | ΑZ, | BA, | BB, | ВG, | BR, | BY, | ΒZ, | CA, | CH, | CN, |
| | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | ES, | FI, | GB, | GD, | GE, | GH, |
| | HR, | HU, | ID, | IL, | IN, | IS, | JΡ, | ΚE, | KG, | KΡ, | KR, | ΚZ, | LC, | LK, | LT, | LU, |
| | LV, | MA, | MD, | MK, | MN, | MX, | NΙ, | NO, | ΝZ, | OM, | PH, | ΡL, | PT, | RO, | RU, | SC, |
| | SE, | SG, | SK, | ТJ, | TM, | TN, | TR, | TT, | UA, | US, | UΖ, | VC, | VN, | ΥU, | ZA, | ZW |
| RW | : AM, | ΑZ, | BY, | KG, | KZ, | MD, | RU, | ТJ, | TM, | ΑT, | BE, | BG, | CH, | CY, | CZ, | DE, |
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| | SI, | SK, | TR | | | | | | | | | | | | | |
| CA 248 | 6557 | | | AA | | 2003 | 1224 | (| CA 2 | 003-2 | 2486 | 557 | | 20 | 00306 | 512 |
| EP 151 | 5717 | | | A1 | | 2005 | 0323 |] | EP 20 | 003- | 7402 | 34 | | 20 | 00306 | 512 |
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| | ΙE, | SI, | LT, | LV, | FI, | RO, | MK, | CY, | AL, | TR, | BG, | CZ, | EE, | HU, | SK | |
| PRIORITY AP | PLN. | INFO | . : | | | | | 1 | US 2 | 002-3 | 3883 | 18P | I | P 20 | 00206 | 513 |
| | | | | | | | | Ī | WO 2 | 003-1 | EP61 | 95 | V | v 20 | 00306 | 512 |
| OTHER SOURCE | E(S): | | | MAR | PAT | 140:4 | 4748 | 0 | | | | | | | | |

The present invention provides calcium salts of indole-derived statins.

More specifically, the invention provides fluvastatin calcium (I), in a highly crystalline form. Furthermore, the present invention is directed to methods for the preparation of I, and to pharmaceutical compns. comprising the crystalline form. The I is effective for the prevention and/or treatment of hypercholesterolemia, hyperlipoproteinemia, dyslipidemia, and atherosclerosis.

IT 634902-71-9P

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of crystalline fluvastatin Ca salt and blood

cholesterol-lowering

effects thereof)

RN 634902-71-9 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

●1/2 Ca

IT 194934-96-8

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of crystalline fluvastatin Ca salt and blood

cholesterol-lowering

effects thereof)

RN 194934-96-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-). Double bond geometry as shown.

đ

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> fil reg COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 5.39 829.71 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE -0.73 -2.92

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3

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 31 AUG 2005 HIGHEST RN 862246-83-1 DICTIONARY FILE UPDATES: 31 AUG 2005 HIGHEST RN 862246-83-1

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

=> => d 123 que stat;fil caplus;s 114 and 123 L18 STR

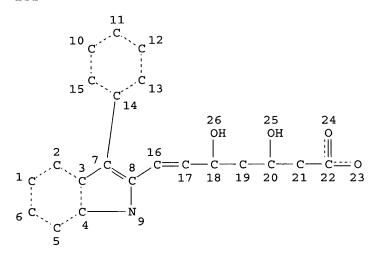
G1 1

VAR G1=NA/LI/K NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 1

STEREO ATTRIBUTES: NONE L21 STR



NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE

L23 92 SEA FILE=REGISTRY SSS FUL L21 AND L18

100.0% PROCESSED 96 ITERATIONS 92 ANSWERS

SEARCH TIME: 00.00.01

| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
|--|-----------------|--------------------|
| FULL ESTIMATED COST | ENTRY 323.09 | SESSION 1152.80 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| CA SUBSCRIBER PRICE | ENTRY 0.00 | SESSION -2.92 |

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FILE COVERS 1907 - 1 Sep 2005 VOL 143 ISS 10 FILE LAST UPDATED: 31 Aug 2005 (20050831/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

27 L14 169 L23

L24 19 L14 AND L23

=> d 1-19 ibib abs hitstr

L24 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:612271 CAPLUS

DOCUMENT NUMBER: 143:115390

TITLE: Process for preparation of statins with high syn to

anti ratio

INVENTOR(S): Lifshitz-Liron, Revital; Perlman, Nurit

PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva

Pharmaceuticals USA, Inc.

SOURCE: PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. | | | | KIND DATE | | | APPLICATION NO. | | | | | | DATE | | | |
|------|------------|------|------|-----|-----------|-----|------|-----------------|-----|------|-----------|------|-----|------|------|------|-----|
| | WO 2005 | 0637 | 28 | | A2 | - | 2005 | 0714 | 1 | WO 2 | 004-1 | US43 | 466 | | 2 | 0041 | 223 |
| | W: | ΑE, | AG, | AL, | AM, | ΑT, | AU, | ΑZ, | BA, | BB, | BG, | BR, | BW, | BY, | ΒZ, | CA, | CH, |
| | | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FI, | GB, | GD, |
| | | GE, | GH, | GM, | HR, | HU, | ID, | ΙL, | IN, | IS, | JP, | ΚE, | KG, | KP, | KR, | KZ, | LC, |
| | | LK, | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NA, | NI, |
| | | NO, | NΖ, | OM, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY, |
| | | ТJ, | TM, | TN, | TR, | TT, | TZ, | UA, | UG, | US, | UΖ, | VC, | VN, | YU, | ZA, | ZM, | ZW |
| | RW: | BW, | GH, | GM, | KE, | LS, | MW, | ΜZ, | NA, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, |
| | | ΑZ, | BY, | KG, | ΚZ, | MD, | RU, | ТJ, | TM, | ΑT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, |
| | | EE, | ES, | FI, | FR, | GB, | GR, | HU, | ΙE, | IS, | ΙT, | LT, | LU, | MC, | NL, | PL, | PT, |
| | | RO, | SE, | SI, | SK, | TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML, |
| | | MR, | ΝE, | SN, | TD, | TG | | | | | | | | | | | |
| | US 2005 | 1596 | 15 | | A1 | | 2005 | 0721 | 1 | US 2 | 004-3 | 2083 | 4 | | 2 | 0041 | 223 |
| PRIO | RITY APP | LN. | INFO | .: | | | | | 1 | US 2 | 003- | 5324 | 58P |] | P 20 | 0031 | 224 |
| | | | | | | | | | 1 | US 2 | 004- | 5477 | 15P |] | P 20 | 0040 | 224 |
| CT | | | | | | | | | | | | | | | | | |

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AB A process was disclosed for reduction of statin ketoesters, such as RCH(Y)CH(OH)CH2COCH2CO2R1 [R = organic radical that is inert to redn and allows for inhibition of 3-hydroxy-3-methylglutaryl CoA; Y = H or forms a double bond with the R group; R1 = alkyl] and purification of the corresponding syn-diol esters syn-RCH(Y)CH(OH)CH2CH(OH)CH2CO2R1 of the statins via selective crystallization Thus, β -keto ester I (R1 = CMe3, R2 = OH, R3R4 = O) was reduced using 9-methoxy-9-borabicyclo[3.3.1]nonane and sodium borohydride in methanol at -70° for 2 h followed by treatment with 30% H2O2 soln to give syn-diol ester I (R1 = CMe3, R2 = R3 = β -OH, R4 = α -H) in 73% yield and 99.0:0.45 d.e. The syn-diol ester was further purified by crystallization and subsequently treated with 47% NaOH to

form

fluvastatin sodium salt I (R1 = Na, R2 = R3 = β -OH, R4 = α -H) in 87% yield.

IT 129332-29-2P

RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(process for preparation of statins with high syn to anti ratio via stereoselective ketone reduction)

RN 129332-29-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

IT 93957-55-2P

RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(process for preparation of statins with high syn to anti ratio via stereoselective ketone reduction)

RN 93957-55-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

IT 93957-53-0

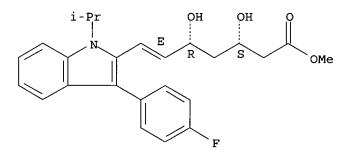
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of statins with high syn to anti ratio via stereoselective ketone reduction)

RN 93957-53-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.



L24 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:474955 CAPLUS

DOCUMENT NUMBER: 143:7598

TITLE: Saponification process for the preparation of

fluvastatin sodium polymorphic crystal form XIV

INVENTOR(S): Frenkel, Gustavo; Gilboa, Eyal

PATENT ASSIGNEE(S): Israel

SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of U.S.

Ser. No. 871,916.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-------------------|------------|
| | | | | |
| US 2005119342 | A1 | 20050602 | US 2004-920112 | 20040817 |
| US 2005038114 | A1 | 20050217 | US 2004-871916 | 20040618 |
| PRIORITY APPLN. INFO.: | | | US 2003-479182P P | 20030618 |
| | | | US 2003-483099P P | 20030630 |
| | | | US 2003-485748P P | 20030710 |
| | | | US 2003-493793P P | 20030811 |
| | | | US 2003-507954P P | 20031003 |
| | | | US 2004-545466P P | 20040219 |
| | | | US 2004-871916 A | 2 20040618 |

AB A process for preparing a polymorphic crystalline form of fluvastatin sodium characterized by a powder X-ray diffraction pattern with peaks at 3.8, 11.1, 12.9, 17.8 and 21.7±0.2 degrees 20 comprises: (A) combining a C1-4 alkyl ester of fluvastatin with acetonitrile at a ratio of about 1:4-6 kgL of the ester to acetonitrile, and with water at a ratio of about 1: 1.3-1:2 kgL of the ester to the water, to obtain a mixture; (B) combining sodium hydroxide with the mixture to saponify the ester obtaining a solution, where if aqueous sodium hydroxide is used, the water ratio does not exceed that provided in step (A); (C) combining addnl. acetonitrile with the solution to precipitate crystalline fluvastatin sodium; and (D) recovering the crystalline

fluvastatin sodium.

IT 93957-53-0 129332-29-2

RL: RCT (Reactant); RACT (Reactant or reagent)

(in a saponification process for the preparation of fluvastatin sodium polymorphic

crystal form XIV)

RN 93957-53-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, (3R,5S,6E)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 129332-29-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

IT 93957-55-2P, Fluvastatin sodium

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (saponification process for the preparation of fluvastatin sodium polymorphic

crystal form XIV)

RN 93957-55-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

Na

L24 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:395268 CAPLUS

DOCUMENT NUMBER: 142:435812

TITLE: Preparation of a polymorph of fluvastatin sodium

INVENTOR(S): Frenkel, Gustavo; Gilboa, Eyal

PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva

Pharmaceuticals USA, Inc.

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| | | | | |
| WO 2005040113 | A1 | 20050506 | WO 2004-US26673 | 20040817 |
| WO 2005040113 | C1 | 20050721 | | |

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              CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
              GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
              NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
              TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
              AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
              SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
              SN, TD, TG
     US 2005038114
                            A1
                                   20050217
                                                US 2004-871916
                                                                          20040618
PRIORITY APPLN. INFO.:
                                                US 2003-507954P
                                                                       P
                                                                          20031003
                                                US 2004-545466P
                                                                      Р
                                                                          20040219
                                                US 2004-871916
                                                                      Α
                                                                          20040618
                                                US 2003-479182P
                                                                      Ρ
                                                                          20030618
                                                US 2003-483099P
                                                                      P
                                                                          20030630
                                                US 2003-485748P
                                                                      Р
                                                                          20030710
                                                US 2003-493793P
                                                                      Ρ
                                                                          20030811
AΒ
     Provided are processes for preparing a polymorphic form of fluvastatin sodium
     with PXRD peaks at 3.8, 11.1, 12.9, 17.8 and 21.7 0.2 degrees two-theta.
ΙT
     93957-55-2P, Fluvastatin sodium 201541-53-9P,
     Fluvastatin sodium monohydrate 851011-47-7P 851011-48-8P
     851011-49-9P 851011-50-2P 851011-51-3P
     851011-52-4P
     RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
         (preparation of a polymorph of fluvastatin sodium)
     93957-55-2 CAPLUS
RN
     6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-
CN
     3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)
```

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 201541-53-9 CAPLUS
CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]3,5-dihydroxy-, monosodium salt, monohydrate, (3R,5S,6E)-rel- (9CI) (CA
INDEX NAME)

● н20

RN 851011-47-7 CAPLUS
CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]3,5-dihydroxy-, monosodium salt, hydrate (2:3), (3R,5S,6E)-rel- (9CI) (CA
INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

●3/2 H₂O

RN 851011-48-8 CAPLUS
CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]3,5-dihydroxy-, monosodium salt, dihydrate, (3R,5S,6E)-rel- (9CI) (CA
INDEX NAME)

●2 H₂O

RN 851011-49-9 CAPLUS
CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]3,5-dihydroxy-, monosodium salt, hydrate (2:5), (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

●5/2 H₂O

RN 851011-50-2 CAPLUS
CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]3,5-dihydroxy-, monosodium salt, trihydrate, (3R,5S,6E)-rel- (9CI) (CA
INDEX NAME)

●3 H₂O

RN 851011-51-3 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]- 3,5-dihydroxy-, monosodium salt, tetrahydrate, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

●4 H₂O

RN 851011-52-4 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, pentahydrate, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

●5 H₂O

IT 93957-53-0

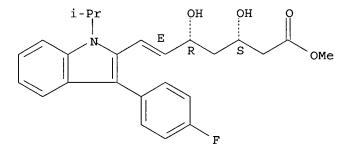
RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of a polymorph of fluvastatin sodium)

RN 93957-53-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1154669 CAPLUS

DOCUMENT NUMBER: 142:79939

TITLE: Preparation of fluvastatin sodium crystal forms for

pharmaceuticals

INVENTOR(S): Revital, Lifshitz-Liron; Tamas, Koltai; Aronhime,

Judith; Perlman, Nurit; Sharon, Avhar-Maydan

PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva

Pharmaceuticals USA, Inc.

SOURCE: PCT Int. Appl., 284 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4 PATENT INFORMATION:

| PATENT N | KIND DATE | | | | APPLICATION NO. | | | | | DATE | | | | | |
|---------------|-----------|--------|-----|-----|-----------------|------|-----|------|-------|-------|------|-----|------|-------|-----|
| WO 20041 | 13292 | | A2 | _ | 2004 | 1229 | Ţ | WO 2 | 004-1 | JS19 | 882 | | 20 | 0040 | 518 |
| W: | AE, A | G, AL, | AM, | AT, | AU, | ΑZ, | BA, | BB, | BG, | BR, | BW, | BY, | ΒZ, | CA, | CH, |
| | CN, C | O, CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FI, | GB, | GD, |
| | GE, G | H, GM, | HR, | HU, | ID, | ΙL, | IN, | IS, | JP, | ΚE, | KG, | KP, | KR, | ΚZ, | LC, |
| | LK, L | R, LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NA, | NI, |
| | NO, N | z, om, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY, |
| | TJ, T | M, TN, | TR, | TT, | TZ, | UA, | UG, | US, | UΖ, | VC, | VN, | ΥU, | ZA, | ZM, | zw |
| RW: | BW, G | H, GM, | KE, | LS, | MW, | MZ, | NA, | SD, | SL, | SZ, | TZ, | UG, | ZM, | ZW, | AM, |
| | AZ, B | Y, KG, | ΚZ, | MD, | RU, | ТJ, | TM, | ΑT, | ВĖ, | BG, | CH, | CY, | CZ, | DE, | DK, |
| | EE, E | S, FI, | FR, | GB, | GR, | HU, | ΙE, | IT, | LU, | MC, | NL, | PL, | PT, | RO, | SE, |
| | SI, S | K, TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GΑ, | GN, | GQ, | GW, | ML, | MR, | NE, |
| | SN, T | D, TG | | | | | | | | | | | | | |
| US 20050 | 32884 | | A1 | | 2005 | 0210 | Ţ | US 2 | 004- | 3720 | 39 | | 20 | 0040 | 518 |
| PRIORITY APPL | N. IN | FO.: | | | | | τ | JS 2 | 003- | 1791 | 32P |] | P 20 | 0030 | 518 |
| | | | | | | | τ | JS 2 | 003- | 4830 | 99P |] | P 20 | 0030 | 630 |
| | | | | | | | Ţ | JS 2 | 003- | 48574 | 48P |] | P 20 | 0030, | 710 |
| | | | | | | | τ | JS 2 | 003- | 1937 | 93P |] | P 20 | 0030 | 311 |
| | | | | | | | Ţ | US 2 | 003- | 5079 | 54 P |] | P 20 | 0031 | 003 |
| | | | | | | | Ţ | JS 2 | 004- | 54546 | 56P |] | P 20 | 00402 | 219 |

AB Provided are crystal forms of fluvastatin sodium and processes for their preparation Thus, fluvastatin Me ester was dissolved in acetone and NaOH solution

in acetone was added. The product, fluvastatin sodium crystal Form I was dried at 50° .

IT 93957-55-2P, Fluvastatin sodium

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (preparation of fluvastatin sodium crystal forms for pharmaceuticals)

RN 93957-55-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

Na

IT 93957-53-0 129332-29-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of fluvastatin sodium crystal forms for pharmaceuticals)

RN 93957-53-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 129332-29-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

L24 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1154668 CAPLUS

DOCUMENT NUMBER: 142:79938

TITLE: Preparation of different crystal forms of fluvastatin

sodium for pharmaceuticals

INVENTOR(S): Revital, Lifshitz-Liron; Koltai, Tamas; Aronhime,

Judith; Perlman, Nurit

PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva

Pharmaceuticals USA, Inc.

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| | | | | |
| WO 2004113291 | A2 | 20041229 | WO 2004-US19879 | 20040618 |
| WO 2004113291 | Α3 | 20050414 | | |

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AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     US 2005032884
                                  20050210
                                              US 2004-872089
                                                                       20040618
                           Α1
PRIORITY APPLN. INFO.:
                                              US 2003-479182P
                                                                    Р
                                                                       20030618
                                              US 2003-483099P
                                                                   Ρ
                                                                       20030630
                                              US 2003-485748P
                                                                   Ρ
                                                                       20030710
                                              US 2003-493793P
                                                                   Р
                                                                       20030811
                                              US 2003-507954P
                                                                   Р
                                                                       20031003
                                              US 2004-545466P
                                                                   Р
                                                                       20040219
AΒ
     Provided are polymorphic forms of fluvastatin sodium and processes for
     their preparation Thus, fluvastatin sodium was suspended in a mixture of
toluene
     and hexane, the mixture was cooled and the product, a crystal form XIV of
     the drug, was obtained.
     93957-55-2P, Fluvastatin sodium
IT
     RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of different crystal forms of fluvastatin sodium for
        pharmaceuticals)
RN
     93957-55-2 CAPLUS
CN
     6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-
     3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)
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Relative stereochemistry.

Double bond geometry as shown.

Na

Relative stereochemistry.

Double bond geometry as shown.

RN 129332-29-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

L24 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1059168 CAPLUS

DOCUMENT NUMBER: 142:38061

TITLE: Preparation of nitrooxy derivatives of fluvastatin,

pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and

anti-platelet activity

INVENTOR(S): Benedini, Francesca; Ongini, Ennio; Del Soldato, Piero

PATENT ASSIGNEE(S): Nicox S. A., Fr.

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PA | rent | NO. | KIN | D : | DATE | | | APPL | ICAT | D | DATE | | | | | | |
|---------------|------|-----|-----|-----|------|-----|------|------|------|------|------|----------|-----|-----|-----|-----|-----|
| | | | | | | | | | | | | | | | | | |
| WO 2004105754 | | | | | A1 | | 2004 | 1209 | 1 | WO 2 | 004- | 20040524 | | | | | |
| | W: | ΑE, | AG, | AL, | AM, | ΑT, | AU, | ΑZ, | BA, | BB, | BG, | BR, | BW, | BY, | BZ, | CA, | CH, |
| | | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FI, | GB, | GD, |
| | | GE, | GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JΡ, | ΚE, | KG, | ΚP, | KR, | ΚZ, | LC, |
| | | LK, | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NA, | NI, |

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NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     US 2005165084
                          A1
                                20050728
                                            US 2004-849561
                                                                    20040520
PRIORITY APPLN. INFO.:
                                            EP 2003-101530
                                                                 A 20030527
OTHER SOURCE(S):
                         MARPAT 142:38061
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Nitrooxy derivs. of therapeutic agents, such as RCO-X-Y-ONO2 [RCO = acyl AB residue of therapeutic agents, including statin acids, such as fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin, ACE inhibitors, angiotensin II receptor antagonists, β -adrenergic blockers, calcium channel blockers, antithrombotics and aspirin; X = 0, S, NR1; Y = linking group, such as, alkylene or phenylene alone or in combination; R1 = H, alkyl], with improved pharmacol. activity and enhanced tolerability were prepared for therapeutic use in treating and/or preventing several diseases, in particular coronary syndromes and neurodegenerative disorders and autoimmune disorders , as well as for reducing cholesterol levels. The vascular disorders for treatment include acute coronary syndromes, stroke, peripheral vascular diseases, disorders associated with endothelial dysfunction, peripheral ischemia, vascular complications in diabetic patients and atherosclerosis. neurodegenerative diseases for treatment include Alzheimer's disease, Parkinson's disease and multiple sclerosis. Thus, ester I was prepared via an esterification reaction of pravastatin sodium with 1,4-dibromobutane n DMF and subsequent treatment of the resulting 4-bromobutanyl pravastatin ester with silver nitrate in MeCN. The prepared nitrooxy statin derivs. were assayed for their ability to induce vasorelaxation, for their effect in vitro on inflammatory pathways, for activity on peripheral vascular disease, for effect on leukocyte adhesion, for antithrombotic activity, for anti-platelet activity, and for inhibition of tissue factor expression.

Ι

IT 803728-75-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(claimed compound; preparation of nitrooxy derivs. of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as

cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and anti-platelet activity)

RN 803728-75-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 2-[2-(nitrooxy)ethoxy]ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

IT 733034-56-5P 803728-42-9P 803728-43-0P 803728-44-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nitrooxy derivs. of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and anti-platelet activity)

RN 733034-56-5 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 4-(nitrooxy)butyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 803728-42-9 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, [4-[(nitrooxy)methyl]phenyl]methyl ester, (3R,5S,6E)-rel-(9CI) (CA INDEX NAME)

RN 803728-43-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, [3-[(nitrooxy)methyl]phenyl]methyl ester, (3R,5S,6E)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 803728-44-1 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, [2-[(nitrooxy)methyl]phenyl]methyl ester, (3R,5S,6E)-rel-(9CI) (CA INDEX NAME)

IT 93957-55-2, Fluvastatin sodium

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nitrooxy derivs. of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and anti-platelet activity)

RN 93957-55-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

IT 803728-87-2P 803728-88-3P 803728-89-4P 803728-90-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of nitrooxy derivs. of fluvastatin, pravastatin, cerivastatin, atorvastatin and rosuvastatin as cholesterol-reducing agents with improved anti-inflammatory, antithrombotic and anti-platelet activity)

RN 803728-87-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 4-bromobutyl ester, (3R,5S,6E)-rel-(9CI) (CA INDEX NAME)

RN 803728-88-3 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, [4-(chloromethyl)phenyl]methyl ester, (3R,5S,6E)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 803728-89-4 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, [3-(chloromethyl)phenyl]methyl ester, (3R,5S,6E)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN803728-90-7 CAPLUS

6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-CN3,5-dihydroxy-, [2-(chloromethyl)phenyl]methyl ester, (3R,5S,6E)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:965217 CAPLUS

DOCUMENT NUMBER: 141:395334

TITLE: Preparation of polymorphic crystalline fluvastatin

sodium

Suri, Sanjay; Sarin, Gurdeep Singh INVENTOR(S): Morepen Laboratories Ltd., India PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PAT | CENT | NO. | | KIND DATE | | | j | APPL | ICAT | DATE | | | | | | | | | | |
|-------|---------------|-------|------|-----------|---------------------|-------------|----------|------|------|------|------|----------|------------|-----|-----|-----|-----|--|--|--|
| WO | WO 2004096765 | | | | | A2 20041111 | | | , | WO 2 | 004- | 20040430 | | | | | | | | |
| WO | 2004096765 | | | | A 3 | | 20050127 | | | | | | | | | | | | | |
| | W: | ΑE, | AG, | AL, | AM, | AT, | AU, | ΑZ, | ВA, | BB, | BG, | BR, | BW, | BY, | ΒZ, | CA, | CH, | | | |
| | | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DΖ, | EC, | EE, | EG, | ES, | FI, | GB, | GD, | | | |
| | | GE, | GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | KE, | KG, | ΚP, | KR, | ΚZ, | LC, | | | |
| | | LK, | LR, | LS, | LT, | LU, | LV, | MA, | MD, | MG, | MK, | MN, | MW, | MX, | MZ, | NA, | NI, | | | |
| | | NO, | NZ, | OM, | PG, | PH, | PL, | PT, | RO, | RU, | SC, | SD, | SE, | SG, | SK, | SL, | SY, | | | |
| | | ТJ, | TM, | TN, | TR, | TT, | TZ, | UA, | UG, | US, | UZ, | VC, | VN, | YU, | ZA, | ZM, | ZW | | | |
| | RW: | BW, | GH, | GM, | ΚE, | LS, | MW, | MZ, | NA, | SD, | SL, | SZ, | TZ, | ÜĠ, | ZM, | ZW, | AM, | | | |
| | | ΑZ, | BY, | KG, | ΚZ, | MD, | RU, | ТJ, | TM, | ΑT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | | | |
| | | EE, | ES, | FI, | FR, | GB, | GR, | HU, | ΙE, | IT, | LU, | MC, | NL, | PL, | PT, | RO, | SE, | | | |
| | | SI, | SK, | TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GA, | GN, | GQ, | GW, | ML, | MR, | ΝE, | | | |
| | | SN, | TD, | TG | | | | | | | | | | | | | | | | |
| ORITY | Y APP | LN. | INFO | . : | IN 2003-DE656 | | | | | | | | A 20030501 | | | | | | | |
| ER SO | OURCE. | (8) . | | | CASREACT 141.395334 | | | | | | | | | | | | | | | |

PRIO

OTHER SOURCE(S): CASREACT 141:395334

Crystalline polymorphic forms of fluvastatin sodium and its hydrates are prepared

by the reaction of the Me ester of fluvastatin with sodium hydroxide followed by the addition of aliphatic ethers (e.g., THF) as an antisolvent to facilitate precipitating the crystal polymorph of fluvastatin sodium.

IT 93957-53-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(in the preparation of polymorphic crystalline fluvastatin sodium)

RN 93957-53-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

IT 93957-55-2P, Fluvastatin sodium 201541-53-9P,

Fluvastatin sodium monohydrate

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (preparation of polymorphic crystalline fluvastatin sodium)

RN 93957-55-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 201541-53-9 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, monohydrate, (3R,5S,6E)-rel-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

● H₂O

L24 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:927170 CAPLUS

DOCUMENT NUMBER: 141:395414

TITLE: Method for separation of optically active

aryldihydroxyheptenoic acid esters

INVENTOR(S): Kudo, Keiko; Tachibana, Kozo; Murazumi, Koichi

PATENT ASSIGNEE(S): Daicel Chemical Industries Ltd., Japan

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. | | | | | | KIND DATE APPLICATION NO. | | | | | | . 01 | DATE | | | | | |
|-------------------------------|------------|------|-------------|-----|------|-----|---------------------------|------|-------|------|----------|------|------|------|-----|------------|------|------|--|
| | | | | | | | | | | | | | | | | | | | |
| | WO | 2004 | A1 20041104 | | | | 1 | WO 2 | - 004 | | 20040423 | | | | | | | | |
| | | W: | ΑE, | AG, | АL, | AM, | AT, | AU, | ΑZ, | BA, | BB, | BG, | BR, | BW, | BY, | ΒZ, | CA, | CH, | |
| | | | CN, | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DZ, | EC, | EE, | EG, | ES, | FI, | GB, | GD, | |
| | | | • | | | | | | IL, | | | | | | | | | | |
| | | | • | • | | - | | | MA, | | | | | | | | | | |
| | | | • | • | • | • | • | • | PT, | • | • | • | | • | | • | | | |
| | | | • | • | • | • | • | • | UA, | • | • | • | | - | | • | | - | |
| | | RW: | BW, | • | , | , | • | | • | | • | • | | | | • | • | | |
| | | | | | | | | | TM, | - | - | | - | - | | | | | |
| | | | • | • | • | | • | • | IE, | • | - | • | | • | • | | • | • | |
| | | | • | | | • | • | • | CI, | • | • | • | • | • | • | • | • | • | |
| | | | , | • | D1 , | ъ, | Q. , | , | C±, | C11, | 011, | O11, | ΟQ, | ···, | , | 1110, | 112, | D11, | |
| TD, TG PRIORITY APPLN. INFO.: | | | | | | | JP 2003-119819 | | | | | | | | 1 | A 20030424 | | | |
| OTHER SOURCE(S): | | | | | | | MARPAT 141:395414 | | | | | | | | | | | | |
| CT | | | | | | | | | | | | | | | | | | | |

GI

AB An optically active aryldihydroxyheptenoic acid ester having an aromatic group (I) [wherein Ar = (un)substituted or optionally fused carbocyclic or heterocyclic aromatic group; R1 = C1-20 alkyl, Ph, C7-18 aralkyl] is separated from a solution containing a mixture of optical isomers of the dihydroxyheptenoic

acid ester by liquid chromatog. with a packing material constituted of a carrier and a polysaccharide derivative supported on the carrier. The polysaccharide derivative is a polysaccharide in which the hydrogen atoms constituting the hydroxyl and amino groups are partially or all replaced by one or more kinds of groups selected from among carbamoyl groups monosubstituted with aromatic groups having specific alkyl groups and benzoyl groups having specific alkyl groups. According to the invention, optically active aryldihydroxyheptenoic acid esters can be separated more distinctly. Thus, (3R,5S,6E)-rel-7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-6-heptenoic acid monosodium salt was extracted from Lescol (NOVARTIS Pharmaceutical Corp.) by CHCl3 at reflux and converted into (3R,5S,6E)-rel-7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1Hindol-2-yl]-3,5-dihydroxy-6-heptenoic acid Me ester (II) by treatment with Me iodide in DMF in the presence of Li2CO3. Cellulose (50 g) was suspended in pyridine, treated with 310 g 4-isopropylphenyl isocyanate, and refluxed for 24 h to give cellulose tris(4-isopropylphenylcarbamate) (III) which was dissolved in acetone, and uniformly poured onto silica gel -(average diameter 20 μm), followed by evaporation of the solvent to give III-supported on silica gel as a packing material. The latter packing material was packed in a stainless steel column (0.46 cm inner diameter X 25 cm length) to give a liquid chromatog. column for separation of optical

Optical isomers of II were separated using the column obtained above and hexane/2-propanol (80/20 volume/volume ratio) as the mobile phase with separation

coefficiency of 2.20.

RN 93957-53-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

RN 615263-37-1 CAPLUS
CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

3,5-dihydroxy-, methyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

RN 786710-22-3 CAPLUS CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

TT 786710-24-5P, (3R,5S,6E)-7-[3-(4-Fluorophenyl)-1-(1-methylethyl)1H-indol-2-yl]-3,5-dihydroxy-6-heptenoic acid ethyl ester
786710-25-6P, (3S,5R,6E)-7-[3-(4-Fluorophenyl)-1-(1-methylethyl)1H-indol-2-yl]-3,5-dihydroxy-6-heptenoic acid ethyl ester
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP
(Preparation)
 (separation of optically active aryldihydroxyheptenoic acid esters by liquid chromatog. resolution using polysaccharide carbamates coated on silica gel)
RN 786710-24-5 CAPLUS
CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

RN 786710-25-6 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:1006762 CAPLUS

DOCUMENT NUMBER: 140:47480

TITLE: Calcium salts of indole derived statins

INVENTOR(S): Chen, Guang-Pei; Kapa, Prasad Koteswara; Sutton, Paul

Allen

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | | KIND | DATE | APPL | ICATION : | NO. | DF | ATE | |
|--------------|---------|---------|----------|---------|-----------|---------|-----|-------|-----|
| | | | | | | | | | |
| WO 200310583 | 7 | A1 | 20031224 | WO 2 | 003-EP61 | 95 | 20 | 00306 | 512 |
| W: AE, | AG, AL, | AM, AT, | AU, AZ | BA, BB, | BG, BR, | BY, BZ, | CA, | CH, | CN, |
| co, | CR, CU, | CZ, DE, | DK, DM | DZ, EC, | EE, ES, | FI, GB, | GD, | GE, | GH, |
| HR, | HU, ID, | IL, IN, | IS, JP | KE, KG, | KP, KR, | KZ, LC, | LK, | LT, | LU, |
| LV, | MA, MD, | MK, MN, | MX, NI | NO, NZ, | OM, PH, | PL, PT, | RO, | RU, | SC, |
| SE, | SG, SK, | TJ, TM, | TN, TR | TT, UA, | US, UZ, | VC, VN, | YU, | ZA, | zw |
| RW: AM, | AZ, BY, | KG, KZ, | MD, RU | TJ, TM, | AT, BE, | BG, CH, | CY, | CZ, | DE, |
| DK, | EE, ES, | FI, FR, | GB, GR | HU, IE, | IT, LU, | MC, NL, | PT, | RO, | SE, |
| SI, | SK, TR | | | | | | | | |

CA 2486557 AΑ 20031224 CA 2003-2486557 20030612 EP 1515717 **A**1 20050323 EP 2003-740234 20030612 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK US 2002-388318P PRIORITY APPLN. INFO.: P 20020613 WO 2003-EP6195 W 20030612

OTHER SOURCE(S): MARPAT 140:47480

AB The present invention provides calcium salts of indole-derived statins.

More specifically, the invention provides fluvastatin calcium (I), in a highly crystalline form. Furthermore, the present invention is directed to methods for the preparation of I, and to pharmaceutical compns. comprising the crystalline form. The I is effective for the prevention and/or treatment of hypercholesterolemia, hyperlipoproteinemia, dyslipidemia, and atherosclerosis.

IT 194934-96-8 634902-72-0 634902-73-1

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of crystalline fluvastatin Ca salt and blood

cholesterol-lowering

effects thereof)

RN 194934-96-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry. Rotation (-). Double bond geometry as shown.

RN 634902-72-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monolithium salt, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

● Li

RN 634902-73-1 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monopotassium salt, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

K

IT 94061-80-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of crystalline fluvastatin Ca salt and blood cholesterol-lowering

effects thereof)

RN 94061-80-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

Na

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:678800 CAPLUS

DOCUMENT NUMBER: 139:214343

TITLE: Process for the manufacture of HMG-CoA reductase

inhibitory mevalonic acid derivatives

INVENTOR(S): Sedelmeier, Gottfried; Mathes, Christian

PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| P | ATENT | NO. | | | KIN | D - | DATE | | i | APPL | ICAT | ION I | NO. | | D. | ATE | |
|---------|--------|------|--------|-----|-----------|--------|------|-------|-----|------|-------|-------|-----|-----|-----|-------|-----|
| W | 2003 | 0707 | 17 | | A1 | - | 2003 | 0828 | 1 | WO 2 | 003- | EP17: | 38 | | 2 | 0030: | 220 |
| | W: | ΑE, | AG, | AL, | AM, | ΑT, | ΑU, | ΑZ, | ΒA, | BB, | BG, | BR, | BY, | ΒZ, | CA, | CH, | CN, |
| | | CO, | CR, | CU, | CZ, | DE, | DK, | DM, | DΖ, | EC, | EE, | ES, | FΙ, | GB, | GD, | GE, | GH, |
| | | HR, | ΗU, | ID, | IL, | IN, | IS, | JP, | ΚE, | KG, | ΚP, | KR, | ΚZ, | LC, | LK, | LT, | LU, |
| | | LV, | MΑ, | MD, | MK, | MN, | MX, | NO, | NZ, | OM, | PH, | PL, | PT, | RO, | RU, | SC, | SE, |
| | | SG, | SK, | ТJ, | TM, | TN, | TR, | TT, | UA, | US, | UΖ, | VC, | VN, | ΥU, | ZA, | ZW | |
| | RW: | AM, | ΑZ, | BY, | KG, | ΚZ, | MD, | RU, | TJ, | TM, | ΑT, | BE, | BG, | CH, | CY, | CZ, | DE, |
| | | DK, | EE, | ES, | FI, | FR, | GB, | GR, | HU, | ΙE, | IT, | LU, | MC, | NL, | PT, | SE, | SI, |
| | | SK, | TR | | | | | | | | | | | | | | |
| C | A 2473 | 075 | | | AA | | 2003 | 0823 | (| CA 2 | 003- | 2473 | 075 | | 2 | 0030 | 220 |
| E | P 1478 | 640 | | | A1 | | 2004 | 1124 |] | EP 2 | 003- | 7147 | 50 | | 2 | 0030 | 220 |
| | R: | AT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | IT, | LI, | LU, | NL, | SE, | MC, | PT, |
| | | ΙE, | SI, | LT, | LV, | FI, | RO, | MK, | CY, | AL, | TR, | BG, | CZ, | EE, | HU, | SK | |
| BI | R 2003 | 0078 | 01 | | Α | | 2004 | 1221 |] | BR 2 | 003- | 7801 | | | 2 | 0030 | 220 |
| J | P 2005 | 5208 | 18 | | T2 | | 2005 | 0714 | , | JP 2 | 003- | 5696 | 24 | | 2 | 0030 | 220 |
| U | S 2005 | 1594 | 80 | | A1 | | 2005 | 0721 | 1 | US 2 | 003- | 5046 | 55 | | 2 | 0030 | 220 |
| PRIORI | TY APP | LN. | INFO | . : | | | | | (| GB 2 | 002- | 4129 | | i | A 2 | 0020 | 221 |
| | | | | | | | | | I | WO 2 | 003-1 | EP17 | 38 | 1 | W 2 | 0030 | 220 |
| OTHER S | SOURCE | (S): | | | MAR | PAT | 139: | 21434 | 43 | | | | | | | | |

OTHER SOURCE(S): MARPAT 139:214343

GI

AΒ Mevalonic acid derivs. I [R = cyclic residue; X = CH2CH2, CH:CH] are prepared by treating R1R2R3P:CHCOCH2CO2R4 [R1-R3 = (un)substituted Ph; R4 = aliphatic, cycloaliph., aromatic] with RCHO, reducing the resulting RCH:CHCOCH2CO2R4 in presence of a chiral metal BINAP or TsDPEN catalyst, treating the resulting alc. with an ester enolate, reducing the second oxo group, and hydrolyzing the ester group. Thus, ClCH2COCH2CO2Et was treated with PPh3 to give Ph3P:CHCOCH2CO2Et which was treated with 2-cyclopropyl-4-(4-fluorophenyl)quinoline-3-carboxaldehyde to give (E) -5-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3-oxopent-4-enoic acid Et ester. This ester was reduced with Ru[(1R,2R)-p-TsNCHPhCHPhNH] $(\eta-p-cymene)$ and treated with Me3COAc to give (E) -(S) -7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-5-hydroxy-3oxohept-4-enoic acid tert.-Bu ester which was reduced with MeOBEt2 and hydrolyzed to give (E)-(3R,5S)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxyhept-4-enoic acid calcium salt.

IT 194934-96-8P 194935-00-7P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (process for the manufacture of HMG-CoA reductase inhibitory mevalonic acid derivs.)

RN 194934-96-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-). Double bond geometry as shown.

RN 194935-00-7 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3S,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-). Double bond geometry as shown.

IT 94061-80-0P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP

(process for the manufacture of HMG-CoA reductase inhibitory mevalonic acid derivs.)

RN94061-80-0 CAPLUS

6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-CN 3,5-dihydroxy-, monosodium salt, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

) Na

REFERENCE COUNT:

10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2003:173584 CAPLUS

DOCUMENT NUMBER:

138:221469

TITLE:

Process for the preparation of indole derivatives

Wolleb, Heinz; Wolleb, Annemarie; Van Der Schaaf, Paul Adriaan; Kolly, Roman; End, Nicole INVENTOR(S):

PATENT ASSIGNEE(S):

Ciba Specialty Chemicals Holding Inc., Switz.

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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20030306
                                              WO 2002-EP9046
     WO 2003018555
                           A1
                                                                         20020813
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
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                                  20030306
                                               CA 2002-2455842
     CA 2455842
                            AΑ
                                                                         20020813
                                               EP 2002-796227
     EP 1423365
                            A1
                                  20040602
                                                                         20020813
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         R:
              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
                                                CN 2002-816435
     CN 1545502
                            Α
                                  20041110
                                                                         20020813
     JP 2005503393
                            T2
                                  20050203
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                                                                         20020813
     US 2005032875
                            A1
                                  20050210
                                                US 2004-487269
                                                                         20040219
PRIORITY APPLN. INFO.:
                                                EP 2001-810817
                                                                     Α
                                                                        20010822
                                                WO 2002-EP9046
                                                                     W
                                                                         20020813
OTHER SOURCE(S):
                          CASREACT 138:221469; MARPAT 138:221469
GI
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- * STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY AVAILABLE VIA OFFLINE PRINT *
- AB A process for the preparation of indole derivs. I [R1 = (un)substituted C1-8-alkyl; R2, R3, R4, R5 = H, (un)substituted C1-8-alkyl, C1-8-alkoxy, phenoxy or benzyloxy, halogen; Y1, Y2 = H, protective group; Y1Y2 = protecting bridge; X1 = H, an organic radical, a cation], in which process a compound II [Z1 = leaving group], is reacted, in the presence of a catalytically effective amount of a palladium catalyst, with a compound III [R6 = H, Br, Cl, I, OSO2CF3, COCI, B(OH)2, a mono- or di-ester derived from -B(OH)2; Y3, Y4 = protecting group; or Y3Y4 = protecting bridge] to form a compound IV and if desired the radicals Y3 and Y4 are converted into the radicals Y1 and Y2 where Y1 and Y2 are hydrogen. Thus, V was prepared from 3-(4-fluorophenyl)-1-isopropylindole via regioselective bromination, reaction with 2-ethoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, palladium-catalyzed coupling with dioxanylacetate VI, deprotection and saponification
- IT 129332-29-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and saponification of; preparation of indole derivs. via palladium-catalyzed

coupling reactions with boronic acid esters)

RN 129332-29-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

IT 93957-55-2P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of indole derivs. via palladium-catalyzed coupling reactions with boronic acid esters)

93957-55-2 CAPLUS RN

6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-CN 3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

REFERENCE COUNT:

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS 6 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

CAPLUS COPYRIGHT 2005 ACS on STN L24 ANSWER 12 OF 19

ACCESSION NUMBER:

2001:886062 CAPLUS

DOCUMENT NUMBER:

136:5904

TITLE:

Process for the preparation of indole derivatives and

intermediates of the process

INVENTOR(S):

Wolleb, Annemarie; Wolleb, Heinz

PATENT ASSIGNEE(S):

Ciba Specialty Chemicals Holding Inc., Switz.

PCT Int. Appl., 44 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| | | | | |
| WO 2001092223 | A1 | 20011206 | WO 2001-EP5667 | 20010517 |

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

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AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
              GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
              LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
              RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT,
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     CA 2407862
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                                                                           20010517
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     AU 2001074049
                             A5
                                    20011211
                                                 AU 2001-74049
     EP 1284964
                             A1
                                    20030226
                                                 EP 2001-940495
                                                                           20010517
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2003535077
                             T2
                                    20031125
                                                 JP 2002-500838
                                                                            20010517
     US 2003166946
                             Α1
                                    20030904
                                                 US 2002-296106
                                                                           20021122
     US 6743926
                             B2
                                    20040601
     US 2004176614
                             A1
                                    20040909
                                                 US 2004-803705
                                                                           20040318
PRIORITY APPLN. INFO.:
                                                 EP 2000-810460
                                                                        Α
                                                                           20000526
                                                 WO 2001-EP5667
                                                                        W
                                                                           20010517
                                                 US 2002-296106
                                                                        A3 20021122
OTHER SOURCE(S):
                            CASREACT 136:5904; MARPAT 136:5904
GI
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AB A process for the preparation of the title compds. I [R1 = C1-C6 alkyl; X = H, hydrocarbon radical or a cation] is reported. E.g., sodium erythro-(±)-(E)-7-[3-(4-fluorophenyl)-1-isopropyl-1H-indol-2-yl]-3,5-dihydroxyhept-6-enoate was prepared in a multistep synthesis from 3-(4-fluorophenyl)-1-isopropyl-1H-indole.

IT 129332-29-2P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of indole derivs.)

Ι

RN 129332-29-2 CAPLUS
CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

IT 93957-55-2P 194934-96-8P 194935-03-0P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of indole derivs.)

RN 93957-55-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 194934-96-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-). Double bond geometry as shown.

RN 194935-03-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:100136 CAPLUS

DOCUMENT NUMBER: 132:260639

TITLE: Mechanism of antioxidative activity of

fluvastatin-determination of the active position

AUTHOR(S): Nakamura, Takashi; Nishi, Hiroyuki; Kokusenya, Yoshio;

Hirota, Kenichi; Miura, Yozo

CORPORATE SOURCE: Analytical Chemistry Department, Product and

Technology Development Laboratory, Tanabe Seiyaku Co.,

Ltd., Osaka, 532-8505, Japan

SOURCE: Chemical & Pharmaceutical Bulletin (2000), 48(2),

235-237

CODEN: CPBTAL; ISSN: 0009-2363 Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal LANGUAGE: English

AB To clarify the mechanism of action for the antioxidative activity of fluvastatin sodium (FLV, (±)-sodium (3RS, 5RS, 6E)-7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-6-heptanoate) and its derivs., reaction of the corresponding Me ester of FLV with di-tert-Bu diperoxyoxalate was examined, and the corresponding keto derivative was isolated from the reaction mixture On the basis of this result, it was concluded that the active site is the allylic carbon conjugated with the

IT 93957-53-0

indole ring.

PUBLISHER:

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)

(mechanism of antioxidative activity of fluvastatin and determination of active

position by reaction of the Me ester with di-tert-Bu diperoxyoxalate) RN 93957-53-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

IT 93957-55-2, Fluvastatin sodium

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(mechanism of antioxidative activity of fluvastatin and determination of active

position by reaction of the Me ester with di-tert-Bu diperoxyoxalate)

RN 93957-55-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:70157 CAPLUS

DOCUMENT NUMBER: 128:140577

TITLE: Synthesis of carbon-14 labeled fluvastatin (Lescol)

AUTHOR(S): Tang, Y. S.; Jones, Lawrence; Sunay, Ustun B.

CORPORATE SOURCE: Chemical Research & Development Department, Novaris

Pharmaceutical Corporation, Hanover, NJ, 07936, USA

SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals

(1998), 41(1), 1-7

CODEN: JLCRD4; ISSN: 0362-4803

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal LANGUAGE: English

GI

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

AB [R*,S*]-(±)-7-[3-(4-Fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl-3-14C]-3,5-dihydroxy-6-heptenoic acid sodium salt (labeled fluvastatin, I) was prepared from [14C]bromoacetyl chloride in a six-step synthesis with an overall radiochem. yield of 13.2%. This synthetic route was chosen because it puts the label in the metabolically stable 3-position of the indole ring.

Ι

IT 202402-41-3P

RN 202402-41-3 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl-3-14C]-3,5-dihydroxy-, monosodium salt, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

IT 202402-39-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of carbon-14 labeled fluvastatin)

RN 202402-39-9 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl-3-14C]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (R*,S*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

REFERENCE COUNT:

14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1997:535638 CAPLUS

DOCUMENT NUMBER:

127:220543

TITLE:

Asymmetric synthesis of 3,5-dihydroxy-6(E)-heptenoate-

containing HMG-CoA reductase inhibitors

AUTHOR (S):

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CORPORATE SOURCE:

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GΙ

AB A one-pot conversion of aldehyde I to hydroxy oxo ester II with high enantioselection, culminating in a practical asym. synthesis of the (3R,5S) isomer (III) of the antihyperlipoproteinemic agent fluvastatin is described. All four 3,5-dihydroxy-6(E)-heptenoate stereoisomers were prepared in enantiopure form starting from II, utilizing selective reduction and

oxidation methods.

IT 194934-96-8P 194934-98-0P 194935-00-7P 194935-03-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(asym. synthesis of 3,5-dihydroxy-6(E)-heptenoate-containing HMG-CoA reductase inhibitors)

RN 194934-96-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-). Double bond geometry as shown.

RN 194934-98-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, [R-[R*,R*-(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

RN 194935-00-7 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3S,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

Page 53

Double bond geometry as shown.

RN 194935-03-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

IT 94061-80-0P 94061-81-1P 194934-99-1P 194935-01-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 94061-80-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

Na

RN 94061-81-1 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-). Double bond geometry as shown.

Na

RN 194934-99-1 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R-[R*,R*-(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

Na

RN 194935-01-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [S-[R*,R*-(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-). Double bond geometry as shown.

Na

REFERENCE COUNT:

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1991:449425 CAPLUS

DOCUMENT NUMBER:

115:49425

TITLE:

Pyrroloquinoline compounds

INVENTOR(S):

Matsuo, Masaaki; Manabe, Takashi; Okumura, Hiroyuki; Matsuda, Hiroshi; Fujii, Naoaki

PATENT ASSIGNEE(S):

Fujisawa Pharmaceutical Co., Ltd., Japan

SOURCE:

Eur. Pat. Appl., 114 pp.

CODEN: EPXXDW

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LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| | | | | |
| EP 414023 | A2 | 19910227 | EP 1990-115042 | 19900804 |
| EP 414023 | A 3 | 19911106 | | |
| R: AT, BE, | CH, DE, DK | , ES, FR, | GB, GR, IT, LI, LU, NI | , SE |
| US 5164400 | Α | 19921117 | US 1990-552127 | 19900713 |
| AU 9060012 | A1 | 19910228 | AU 1990-60012 | 19900731 |
| ZA 9006102 | Α | 19910529 | ZA 1990-6102 | 19900802 |
| CA 2023726 | AA | 19910223 | CA 1990-2023726 | 19900821 |
| NO 9003666 | Α | 19910225 | NO 1990-3666 | 19900821 |
| CN 1049663 | Α | 19910306 | CN 1990-107135 | 19900821 |
| HU 55015 | A2 | 19910429 | HU 1990-5089 | 19900821 |
| JP 03086882 | A2 | 19910411 | JP 1990-221750 | 19900822 |
| PRIORITY APPLN. INFO. | : | | GB 1989-19091 | A 19890822 |
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| omittee cormon (a) | **** | | • | |

OTHER SOURCE(S):

MARPAT 115:49425

GΙ

$$R^{1}$$
 R^{2}
 R^{2}
 R^{3}
 R^{3}

The title 3-hydroxy-3-methylglutaryl-CoA reductase inhibitors I (R1, R2 = H, lower alkyl, R3 = (un)substituted aryl, heteroaryl, R4 = H, halogen, lower alkyl, X = CH2, CH, O, S, SO, SO2, Y = CH2CH2, CH:CH, Z = CH(OH)CH2CH(OH)CH2CO2Na, 6-oxo-4-hydroxytetrahydro-2H-pyran-2-yl) were prepared The ring system was prepared by alkylation of a nitrogen-containing heterocycle with an α -haloketone followed by cyclization. Thus, 2,2-dimethyl-1,2,3,4-tetrahydroquinoline was treated by BrCH2COC6H4F-4 in DMF and then cyclized by ZnO2 in EtOH to give I (R1 = R2 = Me, R3 = 4-FC6H4, R4 = YZ = H, X = CH2).

IT 134397-45-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and cyclization of)

RN 134397-45-8 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

IT 134397-10-7P 134397-11-8P 134397-12-9P 134397-13-0P 134397-14-1P 134397-15-2P 134397-16-3P 134397-18-5P 134397-19-6P 134397-20-9P 134397-21-0P 134397-22-1P 134397-23-2P 134397-24-3P 134397-25-4P 134397-26-5P 134397-27-6P 134397-28-7P 134397-32-3P 134397-30-1P 134397-31-2P 134397-35-6P 134397-36-7P 134397-37-8P

Relative stereochemistry.
Double bond geometry as shown.

RN 134397-11-8 CAPLUS
CN 6-Heptenoic acid, 7-[5,6-dihydro-4,4-dimethyl-1-(3-methylphenyl)-4Hpyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)](9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-12-9 CAPLUS
CN 6-Heptenoic acid, 7-[1-(4-fluorophenyl)-5,6-dihydro-4-methyl-4Hpyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester (9CI) (CA
INDEX NAME)

RN 134397-13-0 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluoro-2-methylphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-14-1 CAPLUS

CN 6-Heptenoic acid, 7-[1-(3,5-dimethylphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-15-2 CAPLUS

CN 6-Heptenoic acid, 7-[5,6-dihydro-4,4-dimethyl-1-(2-naphthalenyl)-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-16-3 CAPLUS

CN 6-Heptenoic acid, 7-[5,6-dihydro-4,4-dimethyl-1-[3-(trifluoromethyl)phenyl]-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-18-5 CAPLUS

CN 6-Heptenoic acid, 7-[1-(3,4-dimethylphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Page 60

RN 134397-19-6 CAPLUS

CN 6-Heptenoic acid, 7-[1-(3,4-dichlorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-20-9 CAPLUS

CN 6-Heptenoic acid, 7-[1-(3-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-21-0 CAPLUS

CN 6-Heptenoic acid, 7-[1-(2,4-difluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

RN 134397-22-1 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluoro-3-methylphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester (9CI) (CA lNDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-23-2 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-chlorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-24-3 CAPLUS

CN 6-Heptenoic acid, 7-[1-(2-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)](9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-25-4 CAPLUS

CN 6-Heptenoic acid, 7-[1-(3,4-difluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij|quinoln-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-26-5 CAPLUS

CN 6-Heptenoic acid, 7-[5,6-dihydro-4,4-dimethyl-1-(4-phenoxyphenyl)-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

RN 134397-27-6 CAPLUS

CN 6-Heptenoic acid, 7-[1-(2,4-dimethylphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9C1) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-28-7 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluorophenyl)-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-29-8 CAPLUS

CN 6-Heptenoic acid, 7-[1-(2,4-difluorophenyl)-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

Relative stereochemistry. Double bond geometry as shown.

134397-30-1 CAPLUS RN

6-Heptenoic acid, 7-[1-(3,4-dimethylpheny])-5,6-dihydro-4H-pyrrolo[3,2,1-CNij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

134397-31-2 CAPLUS RN

6-Heptenoic acid, 7-[1-(3,4-dichlorophenyl)-5,6-dihydro-4H-pyrrolo[3,2,1-CNij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-32-3 CAPLUS
CN 6-Heptenoic acid, 7-[1-(4-fluoro-3-methylphenyl)-5,6-dihydro-4Hpyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)](9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-33-4 CAPLUS
CN 6-Heptenoic acid, 7-[1-(4-fluoro-2-methoxyphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester,
[R*,S*-(E)]- (9CI) (CA INDEX NAME)

Page 66

RN 134397-34-5 CAPLUS

CN 6-Heptenoic acid, 7-[5,6-dihydro-4,4-dimethyl-1-(2,4,6-trifluorophenyl)-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-35-6 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluorophenyl)-5,6-dihydro-4,4,8-trimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

RN 134397-36-7 CAPLUS

CN 6-Heptenoic acid, 7-[8-chloro-1-(4-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-37-8 CAPLUS

CN 6-Heptenoic acid, 7-[8-fluoro-1-(4-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-38-9 CAPLUS

CN 6-Heptenoic acid, 7-[5,6-dihydro-4,4-dimethyl-1-phenyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-39-0 CAPLUS

CN 6-Heptenoic acid, 7-[1-[4-(dimethylamino)phenyl]-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-40-3 CAPLUS

CN 6-Heptenoic acid, 7-[6-(4-fluorophenyl)-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-5-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-41-4 CAPLUS

CN 6-Heptenoic acid, 7-[1-(2-chloro-4-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-42-5 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluoro-2-methoxyphenyl)-5,6-dihydro-4H-

Prepared by: Mary Hale @2-2507 Rem Bldg 1D86

pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

RN 134397-43-6 CAPLUS

CN 6-Heptenoic acid, 7-[5,6-dihydro-1-(2-methoxyphenyl)-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134424-43-4 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluoro-3,5-dimethylphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134424-44-5 CAPLUS

CN 6-Heptenoic acid, 7-[6-(4-fluorophenyl)-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzothiazin-5-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134424-45-6 CAPLUS

CN 6-Heptenoic acid, 7-[1-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134774-67-7 CAPLUS
CN 6-Heptenoic acid, 7-[1-(4-fluorophenyl)-4,4-dimethyl-4H-pyrrolo[3,2,1ij]quinolin-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA
INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of) 134397-46-9 CAPLUS

RN 134397-46-9 CAPLUS
CN 6-Heptenoic acid, 7-[5,6-dihydro-4,4-dimethyl-1-(3-methylphenyl)-4Hpyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt,
[R*,S*-(E)]- (9CI) (CA INDEX NAME)

Na

RN 134397-47-0 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluorophenyl)-5,6-dihydro-4-methyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt (9CI) (CA INDEX NAME)

Na

RN 134397-48-1 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluoro-2-methylphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-49-2 CAPLUS

CN 6-Heptenoic acid, 7-[1-(3,5-dimethylphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-50-5 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluoro-3,5-dimethylphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-51-6 CAPLUS

CN 6-Heptenoic acid, 7-[5,6-dihydro-4,4-dimethyl-1-(2-naphthalenyl)-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-52-7 CAPLUS

CN 6-Heptenoic acid, 7-[5,6-dihydro-4,4-dimethyl-1-[3-(trifluoromethyl)phenyl]-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-54-9 CAPLUS

CN 6-Heptenoic acid, 7-[1-(3,4-dimethylphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-55-0 CAPLUS

CN 6-Heptenoic acid, 7-[1-(3,4-dichlorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-56-1 CAPLUS

CN 6-Heptenoic acid, 7-[1-(3-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-57-2 CAPLUS

CN 6-Heptenoic acid, 7-[1-(2,4-difluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 134397-58-3 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluoro-3-methylphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-59-4 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-chlorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-60-7 CAPLUS

CN 6-Heptenoic acid, 7-[1-(2-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-61-8 CAPLUS

CN 6-Heptenoic acid, 7-[1-(3,4-difluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 134397-62-9 CAPLUS

CN 6-Heptenoic acid, 7-[5,6-dihydro-4,4-dimethyl-1-(4-phenoxyphenyl)-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-63-0 CAPLUS

CN 6-Heptenoic acid, 7-[1-(2,4-dimethylphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-64-1 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluorophenyl)-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-65-2 CAPLUS

CN 6-Heptenoic acid, 7-[1-(2,4-difluorophenyl)-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 134397-66-3 CAPLUS

CN 6-Heptenoic acid, 7-[1-(3,4-dimethylphenyl)-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-67-4 CAPLUS

CN 6-Heptenoic acid, 7-[1-(3,4-dichlorophenyl)-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-68-5 CAPLUS
CN 6-Heptenoic acid, 7-[1-(4-fluoro-3-methylphenyl)-5,6-dihydro-4H-

pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt,
[R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-69-6 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluoro-2-methoxyphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-70-9 CAPLUS

CN 6-Heptenoic acid, 7-[5,6-dihydro-4,4-dimethyl-1-(2,4,6-trifluorophenyl)-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-71-0 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluorophenyl)-5,6-dihydro-4,4,8-trimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-72-1 CAPLUS

CN 6-Heptenoic acid, 7-[8-fluoro-1-(4-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-73-2 CAPLUS

CN 6-Heptenoic acid, 7-[5,6-dihydro-4,4-dimethyl-1-phenyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-74-3 CAPLUS

CN 6-Heptenoic acid, 7-[1-[4-(dimethylamino)phenyl]-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-75-4 CAPLUS

CN 6-Heptenoic acid, 7-[6-(4-fluorophenyl)-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzoxazin-5-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-76-5 CAPLUS

CN 6-Heptenoic acid, 7-[6-(4-fluorophenyl)-2,3-dihydropyrrolo[1,2,3-de]-1,4-benzothiazin-5-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-77-6 CAPLUS

CN 6-Heptenoic acid, 7-[6-(4-fluorophenyl)-2,3-dihydro-1-oxidopyrrolo[1,2,3-de]-1,4-benzothiazin-5-yl]-3,5-dihydroxy-, monosodium salt, (3R*,5S*,6E)-(9CI) (CA INDEX NAME)

RN 134397-78-7 CAPLUS

CN 6-Heptenoic acid, 7-[6-(4-fluorophenyl)-2,3-dihydro-1,1-dioxidopyrrolo[1,2,3-de]-1,4-benzothiazin-5-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-79-8 CAPLUS

CN 6-Heptenoic acid, 7-[1-(2-chloro-4-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-80-1 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluoro-2-methoxyphenyl)-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 134397-81-2 CAPLUS

CN 6-Heptenoic acid, 7-[5,6-dihydro-1-(2-methoxyphenyl)-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134397-88-9 CAPLUS

CN 6-Heptenoic acid, 7-[6-(4-fluorophenyl)-2,3-dihydro-1-oxidopyrrolo[1,2,3-de]-1,4-benzothiazin-5-yl]-3,5-dihydroxy-, methyl ester, (3R*,5S*,6E)-(9CI) (CA INDEX NAME)

RN 134397-89-0 CAPLUS

CN 6-Heptenoic acid, 7-[6-(4-fluorophenyl)-2,3-dihydro-1,1-dioxidopyrrolo[1,2,3-de]-1,4-benzothiazin-5-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 134397-92-5 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]-(-)- (9CI) (CA INDEX NAME)

Rotation (-). Absolute stereochemistry unknown. Double bond geometry as shown.

Na

RN 134397-93-6 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown. Double bond geometry as shown.

Na

RN 134397-97-0 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluoro-2-methoxyphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]-(-)- (9CI) (CA INDEX NAME)

Rotation (-). Absolute stereochemistry unknown. Double bond geometry as shown.

RN 134424-46-7 CAPLUS

CN 6-Heptenoic acid, 7-[8-chloro-1-(4-fluorophenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

Na

RN 134424-47-8 CAPLUS

CN 6-Heptenoic acid, 7-[1-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]-5,6dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-,
monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

RN 134774-68-8 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluorophenyl)-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

IT 134397-98-1P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as hydroxymethylglutaryl-CoA reductase inhibitor)

RN 134397-98-1 CAPLUS

CN 6-Heptenoic acid, 7-[1-(4-fluoro-2-methoxyphenyl)-5,6-dihydro-4,4-dimethyl-4H-pyrrolo[3,2,1-ij]quinolin-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]-(+)- (9CI) (CA INDEX NAME)

Rotation (+). Absolute stereochemistry unknown. Double bond geometry as shown.

L24 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1990:531998 CAPLUS

DOCUMENT NUMBER: 113:131998

TITLE: Stereoselective preparation of erythro-E-3,5-dihydroxy-

7-[3'(4"-fluorophenyl)-1'(1"-methylethyl)indol-

2'yl]heptenoates

INVENTOR(S): Chen, Kau Ming; Kapa, Prasad Koteswara; Lee, George

T.; Repic, Oljan; Hess, Petr; Crevoisier, Michel

PATENT ASSIGNEE(S): Sandoz A.-G., Switz.; Sandoz-Patent-G.m.b.H.;

Sandoz-Erfindungen-Verwaltungsgesellschaft m.b.H.

SOURCE: Eur. Pat. Appl., 39 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| | | | | | APPLICATION NO. | | | | |
|-----|----------|-----|-----|-----|-----------------|------------------------|----------|--|--|
| | | | | | | | | | |
| | | | | | | EP 1989-118906 | 19891011 | | |
| EΡ | 363934 | | | B1 | 19931229 | | | | |
| | R: AT, | BE, | CH, | DE, | ES, FR, GB, | GR, IT, LI, LU, NL, SI | Ξ | | |
| WO | 9003962 | | | A1 | 19900419 | WO 1989-EP1201 | 19891011 | | |
| | W: AU, | BG, | DK, | FI, | HU, JP, KR, | NO, RO, SU | | | |
| ΑU | 8943448 | • | · | A1 | 19900501 | AU 1989-43448 | 19891011 | | |
| ΑU | 636122 | | | B2 | 19930422 | | | | |
| HU | 53860 | | | A2 | 19901228 | HU 1989-6048 | 19891011 | | |
| | 207993 | | | | | | | | |
| | 03501735 | | | | | JP 1989-510605 | 19891011 | | |
| | 2853227 | | | | | | | | |
| | | | | | | EP 1993-106005 | 19891011 | | |
| | 562643 | | | | | | | | |
| | | | | | | GR, IT, LI, LU, NL, SI | Ξ | | |
| ΔТ | 99281 | , | , | E, | 19940115 | AT 1989-118906 | 19891011 | | |
| TT. | 91941 | | | Δ1 | 19941021 | IL 1989-91941 | 19891011 | | |
| | 2060712 | | | | | ES 1989-118906 | | | |
| | | | | B1 | | RO 1989-145326 | | | |
| | | | | | | | | | |
| | 2051907 | | | | | RU 1989-4830164 | | | |
| | | | | | | CA 1989-2000553 | 19891012 | | |
| | | | | | 20011204 | | | | |
| DD | 296908 | | | A5 | 19911219 | DD 1989-333538 | 19891012 | | |

| CZ | 283316 | B6 | 19980218 | CZ | 1989-5797 | | 19891012 |
|----------|---------------|----|----------|----|-------------|---|----------|
| SK | 280845 | B6 | 20000814 | SK | 1989-5797 | | 19891012 |
| ZA | 8907782 | A | 19910925 | za | 1989-7782 | | 19891013 |
| US | 5189164 | Α | 19930223 | US | 1990-482433 | | 19900220 |
| NO | 9002598 | Α | 19900807 | NO | 1990-2598 | | 19900612 |
| NO | 174623 | В | 19940228 | | | | |
| NO | 174623 | C | 19940608 | | | | |
| FΙ | 98063 | В | 19961231 | FΙ | 1990-2935 | | 19900612 |
| FI | 98063 | С | 19970410 | | | | |
| DK | 9001446 | Α | 19900613 | DK | 1990-1446 | | 19900613 |
| DK | 175073 | B1 | 20040524 | | | | |
| PRIORITY | APPLN. INFO.: | | | US | 1988-257475 | Α | 19881013 |
| | | | | US | 1989-355531 | Α | 19890522 |
| | | | | ΕP | 1989-118906 | Α | 19891011 |
| | | | | WO | 1989-EP1201 | Α | 19891011 |
| | | | | | | | |

OTHER SOURCE(S):

MARPAT 113:131998

GΙ

Me Me

The title compds. (I; R = organic group inert to reducing conditions; R1 = ester group inert to the reaction conditions; X = CH2CH2, CH:CH) were prepared by stereoselective reduction of II (one of X1,X2 = 0, the other = H, OH) using R4OBR23 (R3 = primary or secondary C2-4 alkyl, R4 = allyl, C1-4 alkyl) and NaBH4 in a mixed alc./THF solvent followed by cleavage of the intermediate cyclic boronate. Thus, (±)-E-1-[3'-(4''-fluorophenyl)-1'-(1''-methylethyl)indol-2'-yl]-5-hydroxy-3-oxohept-6-enoic acid tert-Bu ester in THF/MeOH at -74 to -77° was added dropwise to a mixture of NaBH4 and MeOBEt2 in THF/MeOH. The mixture was stirred 30 min to give a cyclic boronate which in EtOAc was treated with 30% H2O2 to give racemic diol III (99.67% erythro).

III

IT 93957-55-2P

RN 93957-55-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

IT 93957-53-0P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, via stereoselective reduction of hydroxyketo ester)

RN 93957-53-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

IT 129332-29-2

RL: RCT (Reactant); RACT (Reactant or reagent) (stereoselective preparation and hydrolysis of)

RN 129332-29-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, 1,1-dimethylethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

L24 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1986:460752 CAPLUS

DOCUMENT NUMBER: 105:60752

TITLE: Silylated dihydroxyoxohexanoate intermediates for

6-substituted-4-hydroxytetrahydropyran-2-ones

INVENTOR(S): Kapa, Prasad K.
PATENT ASSIGNEE(S): Sandoz, Inc., USA

SOURCE: U.S., 9 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | AP | PLICATION NO. | | DATE |
|------------------------|--------|--------------|----|---------------|----|----------|
| | | | | | | |
| US 4571428 | Α | 19860218 | US | 1983-512163 | | 19830708 |
| US 4841071 | Α | 19890620 | US | 1985-771809 | | 19850903 |
| PRIORITY APPLN. INFO.: | | | US | 1983-512163 | Α3 | 19830708 |
| OTHER SOURCE(S): | CASREA | CT 105:60752 | | | | |
| GI | | | | | | |

The title intermediates (I; R = OH-protective group; R1 = C1-4 alkyl, PhCH2), precursors for antiatherosclerotic (no data) hydroxytetrahydropyranones (e.g., II), were prepared Thus, hydrogenation of phloroglucinol over Raney Ni gave cis-1,3,5-trihydroxycyclohexane, which was diprotected with Me3CSiPh2Cl and oxidized with pyridinium chlorochromate (III) to give the corresponding silylated dihydroxycyclohexanone. The latter underwent Baeyer-Villiger oxidation, followed by methanolysis and reoxidn. with III, to give I (R = SiPh2CMe3, R1 = Me) (IV). Wittig reaction of IV with PhCH2P+Ph3 Cl-, followed by deprotection and lactonization, gave II. IV was utilized as an intermediate for other antiatherosclerotics via Wittig reaction with appropriate phosphonium salts.

IT 103338-14-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and hydrolysis of)

RN 103338-14-3 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

IT 103338-13-2P

RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as antiatherosclerotic)

RN 103338-13-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

L24 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1985:24475 CAPLUS

DOCUMENT NUMBER: 102:24475

TITLE: Analogs of mevalolactone and derivatives thereof and

their use as pharmaceuticals

INVENTOR(S): Kathawala, Faizulla Gulamhusein

PATENT ASSIGNEE(S): Sandoz A.-G., Switz.
SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

| P | PATENT NO. | | | | KIND | | DATE | | PLICATION NO. | | DATE | |
|--------|--|-----|------|-----|------------|----|-----------|-------|----------------------------|---|------------|--|
| W | 84021 W: | .31 | | | A1 | | 19840607 | | 1983-EP308 | | | |
| ΔI | 1 83226 | 12, | DIC, | 11, | 110, A1 | O. | 19840618 | ΔIJ | 1983-22612 | | 19831118 | |
| ΔI | J 83226 J 57002 P 60500 P 02046 | 1 | | | B2 | | 19880303 | | 1700 00010 | | 17001110 | |
| J | 60500 | 015 | | | T2 | | 19850110 | | 1983-503754 | | 19831118 | |
| J | 02046 | 031 | | | B4 | | 19901012 | | | | | |
| Н | J 35642 | } | | | 0 | | 19850729 | HU | 1984-284 | | 19831118 | |
| | J 20425 | 3 | | | В | | 19911230 | | | | | |
| E | 5 52742 | 8 | | | A 1 | | 19850801 | ES | 1983-527428 | | 19831121 | |
| | 70286 | | | | | | | IL | 1983-70286 | | 19831121 | |
| E | 11402 | 27 | | | A1 | | 19840725 | EP | 1983-810548 | | 19831122 | |
| E | 11402 | :7 | | | B1 | | 19880107 | | | | | |
| | R: | ΑT, | BE, | CH, | DE, | FR | , GB, IT, | LI, L | U, NL, SE | | | |
| Zi | A 83087 A 12104 F 31718 F 84026 | 18 | | | Α | | 19850828 | ZA | 1983-8718 | | 19831122 | |
| C | 12104 | 05 | | | A1 | | 19860826 | CA | 1983-441684 1983-810548 | | 19831122 | |
| A. | r 31718 | } | | | E | | 19880115 | AT | 1983-810548 | | 19831122 | |
| F | 84026 | 15 | | | Α | | 19840628 | FI | 1984-2615 | | 19840628 | |
| F. | I 77228 | } | | • | В | | 19881031 | | | | | |
| | 77228 | | | | | | 19890210 | | | | | |
| Di | K 84035 | 92 | | | Α | | 19840720 | DK | 1984-3592 | | 19840720 | |
| | 3 47390 | | | | | | 19880419 | | 1985-707854 | | | |
| D1 | K 90009 | 78 | | | Α | | 19900419 | DK | 1990-978 | | 19900419 | |
| Di | K 16524 | 4 | | | В | | 19921026 | | | | | |
| Di | K 16524 | : 4 | | | С | | 19930322 | | | | | |
| | 03047 | | | | A2 | | 19910228 | JP | 1990-120164 | | 19900511 | |
| | 04040 | | | | B4 | | 19920702 | | | | | |
| | 5 53547 | | | | Α | | 19941011 | US | 1993-157595 | | 19931124 | |
| PRIORI | ry appi | .N. | INFO | .: | | | | | 1982-443668 | | | |
| | | | | | | | | | 1983-548850 | | | |
| | | | | | | | | | 1983-EP308 | | | |
| | | | | | | | | | 1983-810548 | | | |
| | | | | | | | | | 1985-707854 | | | |
| | | | | | | | | US | 1985-722288 | В | 1 19850411 | |
| CT. | | | | | | | | | | | | |

GΙ

$$R^5$$
 R^1
 R^1
 R^2
 R^3
 R^3
 R^3
 R^3
 R^4
 R^3
 R^4
 R^7
 R^7
 R^7
 R^7
 R^7
 R^7
 R^7
 R^7

AB Antiatherosclerotic (no data) indoles I [R, R1 = Ph, substituted Ph, alkyl, cycloalkyl, aralkyl; R2 = H, alkyl; R3 = OH, R4 = H; R3R4 = bond; R5, R6 = H, alkyl, cycloalkyl, alkoxy, CF3, F, Cl, PhO, PhCH2O; X = (CH2)0-3, CH:CH] were prepared Thus, II (R7 = CO2Et) was reduced to the alc. and reoxidized to the aldehyde which was treated with Bu3SnCH:CHOEt to give II (R7 = E-CH:CHCHO). The latter compound was treated with MeCOCH2CO2Me to give II [R7 = E-CH:CHCH(OH)CH2COCH2CO2Me] was was reduced to diol, followed by ester hydrolysis, to give II [R7 = E-CH:CHCH(OH)CH2CH(OH)CH2CO2H]. Lactonization of this acid gave I [X = E-CH:CH, R = Me; R2 = R5 = R6 = H, R1 = 4-FC6H4, R3R4 = bond].

Relative stereochemistry.

Double bond geometry as shown.

RN 93957-53-0 CAPLUS
CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]3,5-dihydroxy-, methyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

93936-57-3P 93936-58-4P 93936-59-5P IT 93936-60-8P 93936-61-9P 93936-62-0P 93936-63-1P 93936-64-2P 93936-65-3P 93936-66-4P 93936-67-5P 93936-68-6P 93936-69-7P 93936-70-0P 93936-71-1P 93936-72-2P 93936-73-3P 93936-74-4P 93936-75-5P 93936-76-6P 93936-77-7P 93936-78-8P 93936-79-9P 93936-80-2P 93936-81-3P 93936-82-4P 93936-83-5P 93936-84-6P 93936-85-7P 93936-86-8P 93936-87-9P 93937-46-3P 93937-47-4P 93937-50-9P 93937-51-0P 93937-52-1P 93937-53-2P 93937-54-3P 93937-55-4P 93937-56-5P 93937-57-6P 93937-58-7P 93937-59-8P 93937-60-1P 93937-61-2P 93937-62-3P 93937-63-4P 93937-64-5P 93937-65-6P 93937-66-7P 93937-67-8P 93937-68-9P 93957-55-2P 93957-58-5P

Relative stereochemistry.

Double bond geometry as shown.

RN 93936-58-4 CAPLUS
CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-7-(phenylmethoxy)-1H indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

Na

RN 93936-59-5 CAPLUS
CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-7-(phenylmethoxy)-1H indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-60-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-5-(phenylmethoxy)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93936-61-9 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(2-phenylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

RN 93936-62-0 CAPLUS

Page 102

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(2-phenylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-63-1 CAPLUS

CN 6-Heptenoic acid, 7-[1-ethyl-3-(4-fluorophenyl)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93936-64-2 CAPLUS

CN 6-Heptenoic acid, 7-[1-ethyl-3-(4-fluorophenyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 93936-65-3 CAPLUS

CN 6-Heptenoic acid, 7-[1-ethyl-3-(4-fluorophenyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-66-4 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-4,6-dimethyl-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Page 104

RN 93936-67-5 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-4,6-dimethyl-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-68-6 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-4,6-dimethyl-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-69-7 CAPLUS

CN 6-Heptenoic acid, 7-[3-(3,5-dimethylphenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 93936-70-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(3,5-dimethylphenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-71-1 CAPLUS

CN 6-Heptenoic acid, 7-[5-cyclohexyl-3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Page 106

RN 93936-72-2 CAPLUS

CN 6-Heptenoic acid, 7-[5-cyclohexyl-3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-73-3 CAPLUS

CN 6-Heptenoic acid, 7-[5-cyclohexyl-3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-74-4 CAPLUS

CN 6-Heptenoic acid, 7-[1-cyclohexyl-3-(4-fluorophenyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 93936-75-5 CAPLUS

CN 6-Heptenoic acid, 7-[1-cyclohexyl-3-(4-fluorophenyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-76-6 CAPLUS

CN 6-Heptenoic acid, 7-[1-cyclohexyl-3-(4-fluorophenyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 93936-77-7 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-6-(phenylmethoxy)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,R*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93936-78-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluoro-3,5-dimethylphenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

RN 93936-79-9 CAPLUS

CN 6-Heptenoic acid, 3,5-dihydroxy-7-[1-(1-methylethyl)-3-(2-methylphenyl)-1H-indol-2-yl]-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-80-2 CAPLUS

CN 6-Heptenoic acid, 3,5-dihydroxy-7-[1-(1-methylethyl)-3-(2-methylphenyl)-1H-indol-2-yl]-, monosodium salt, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

● №а

RN 93936-81-3 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluoro-3-methylphenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-82-4 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluoro-3-methylphenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93936-83-5 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluoro-3,5-dimethylphenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-84-6 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-6-(phenylmethoxy)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93936-85-7 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1,4,6-tris(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93936-86-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(2-methylpropyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93936-87-9 CAPLUS

Page 113

CN 6-Heptenoic acid, 7-[3-(4-fluoro-2-methylphenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93937-46-3 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluoro-2-methylphenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-47-4 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(2-methylpropyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-50-9 CAPLUS

CN 6-Heptenoic acid, 3,5-dihydroxy-7-(1-methyl-3-phenyl-1H-indol-2-yl)-, ethyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-51-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-6-(phenylmethoxy)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-52-1 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-6-(phenylmethoxy)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-53-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(3,4-dimethylphenyl)-1-methyl-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-54-3 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-4-(phenylmethoxy)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-55-4 CAPLUS

CN 6-Heptenoic acid, 7-[3-(3,5-dimethylphenyl)-1-methyl-1H-indol-2-yl]-3,5-

dihydroxy-, ethyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-56-5 CAPLUS

CN 6-Heptenoic acid, 7-[5-chloro-3-(4-fluorophenyl)-1-methyl-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-57-6 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-5-methoxy-1-methyl-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-58-7 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-7-(phenylmethoxy)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,S*-(E)]- (9CI) (CA INDEX

Page 117

NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-59-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-5-(phenylmethoxy)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-60-1 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(2-phenylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-61-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-4,6-dimethyl-1-(1-methylethyl)-1H-

indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-62-3 CAPLUS

CN 6-Heptenoic acid, 7-[3-(3,5-dimethylphenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-63-4 CAPLUS

CN 6-Heptenoic acid, 7-[5-cyclohexyl-3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-64-5 CAPLUS

CN 6-Heptenoic acid, 7-[1-cyclohexyl-3-(4-fluorophenyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-65-6 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-6-(phenylmethoxy)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,S*-(E)]-(9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-66-7 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluoro-3,5-dimethylphenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-67-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluoro-2-methylphenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93937-68-9 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(2-methylpropyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93957-55-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93957-58-5 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93957-66-5 CAPLUS

CN 6-Heptenoic acid, 3,5-dihydroxy-7-(1-methyl-3-phenyl-1H-indol-2-yl)-, ethyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93957-67-6 CAPLUS

Page 122

CN 6-Heptenoic acid, 3,5-dihydroxy-7-(1-methyl-3-phenyl-1H-indol-2-yl)-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93957-68-7 CAPLUS

CN 6-Heptenoic acid, 3,5-dihydroxy-7-(1-methyl-3-phenyl-1H-indol-2-yl)-, monosodium salt, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93957-69-8 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-6-(phenylmethoxy)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93957-70-1 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-6-(phenylmethoxy)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93957-71-2 CAPLUS

CN 6-Heptenoic acid, 7-[3-(3,4-dimethylphenyl)-1-methyl-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93957-72-3 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93957-73-4 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-4-(phenylmethoxy)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93957-74-5 CAPLUS

CN 6-Heptenoic acid, 7-[3-(3,5-dimethylphenyl)-1-methyl-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93957-75-6 CAPLUS

CN 6-Heptenoic acid, 7-[3-(3,5-dimethylphenyl)-1-methyl-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93957-76-7 CAPLUS

CN 6-Heptenoic acid, 7-[3-(3,5-dimethylphenyl)-1-methyl-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

Na

RN 93957-77-8 CAPLUS

CN 6-Heptenoic acid, 7-[5-chloro-3-(4-fluorophenyl)-1-methyl-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93957-78-9 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-5-methoxy-1-methyl-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,R*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 93984-61-3 CAPLUS

CN 6-Heptenoic acid, 7-[1-ethyl-3-(4-fluorophenyl)-1H-indol-2-yl]-3,5-dihydroxy-, ethyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

RN 94061-80-0 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+). Double bond geometry as shown.

RN

94061-81-1 CAPLUS 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-(1-methylethyl)-1H-indol-2-yl]-CN3,5-dihydroxy-, monosodium salt, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-). Double bond geometry as shown.

Na

RN103338-13-2 CAPLUS

6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-1H-indol-2-yl]-3,5dihydroxy-, monosodium salt, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry as shown.

RN 103338-14-3 CAPLUS

CN 6-Heptenoic acid, 7-[3-(4-fluorophenyl)-1-methyl-1H-indol-2-yl]-3,5-dihydroxy-, methyl ester, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

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                              Sutton, Paul Allen
PATENT ASSIGNEE(S):
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               CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC,
          SE, SG, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VC, VN, YU, ZA, ZW RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
               SI, SK, TR
      CA 2486557
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                                      20050323
                                                    EP 2003-740234
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               AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
                                                     US 2002-388318P P 20020613
WO 2003-EP6195 W 20030612
PRIORITY APPLN. INFO.:
OTHER SOURCE(S):
                             MARPAT 140:47480
      The present invention provides calcium salts of
      indole-derived statins. More specifically, the invention provides
fluvastatin calcium (I), in a highly crystalline form. Furthermore, the
      present invention is directed to methods for the preparation of I, and to
      pharmaceutical compns. comprising the crystalline form. The I is effective for
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REFERENCE COUNT:

L29 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN

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the prevention and/or treatment of hypercholesterolemia, hyperlipoproteinemia, dyslipidemia, and atherosclerosis.

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Page 130

=> dis his ful (FILE 'HOME' ENTERED AT 16:46:00 ON 01 SEP 2005) FILE 'REGISTRY' ENTERED AT 16:46:07 ON 01 SEP 2005 L1STR 13 SEA SSS SAM L1 L2 L3 STR O SEA SSS SAM L1 AND L3 L4L5 2 SEA SSS FUL L1 AND L3 D L5 QUE STAT FILE 'CAPLUS' ENTERED AT 16:48:34 ON 01 SEP 2005 3 SEA ABB=ON PLU=ON L5 L6 D 1-3 IBIB ABS HITSTR S L1 FILE 'REGISTRY' ENTERED AT 16:49:30 ON 01 SEP 2005 L7 305 SEA SSS FUL L1 FILE 'CAPLUS' ENTERED AT 16:49:30 ON 01 SEP 2005 1294 SEA ABB=ON PLU=ON L7 L8 FILE 'REGISTRY' ENTERED AT 16:49:44 ON 01 SEP 2005 L9 305 SEA SSS FUL L1 L10 STR L1 L11 STR L10 L12 6 SEA SSS SAM L10 0 SEA SSS SAM L11 L13 113 SEA SSS FUL L10 L140 SEA SSS FUL L11 L15 D L14 QUE STAT D L15 QUE STAT FILE 'CAPLUS' ENTERED AT 16:51:48 ON 01 SEP 2005 1 SEA ABB=ON PLU=ON L14 AND L5 L16 D IBIB ABS HITSTR FILE 'REGISTRY' ENTERED AT 16:52:05 ON 01 SEP 2005 L17 STR L11 L18 STR O SEA SSS SAM L17 AND L18 L19 O SEA SSS FUL L17 AND L18 L20 L21 STR L17 4 SEA SSS SAM L21 AND L18 L2292 SEA SSS FUL L21 AND L18 L23 D L23 QUE STAT FILE 'CAPLUS' ENTERED AT 16:53:35 ON 01 SEP 2005 19 SEA ABB=ON PLU=ON L14 AND L23 L24 D 1-19 IBIB ABS HITSTR FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 16:54:31 ON 01 SEP 2005 L25 O SEA ABB=ON PLU=ON CHEN G?/AU AND INDOLE(L)CALCIUM SALT? O SEA ABB=ON PLU=ON CHEN G?/AU AND INDOLE(L)CALCIUM SALT? L26 O SEA ABB=ON PLU=ON CHEN G?/AU AND INDOLE(L)CALCIUM SALT? L27

1 SEA ABB=ON PLU=ON CHEN G?/AU AND INDOLE(L)CALCIUM SALT?

1 SEA ABB=ON PLU=ON CHEN G?/AU AND INDOLE(L) CALCIUM SALT?

D IBIB ABS

TOTAL FOR ALL FILES

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FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 31 AUG 2005 HIGHEST RN 862246-83-1 DICTIONARY FILE UPDATES: 31 AUG 2005 HIGHEST RN 862246-83-1

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Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

FILE CAPLUS

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FILE MEDLINE

FILE LAST UPDATED: 31 AUG 2005 (20050831/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/ http://www.nlm.nih.gov/pubs/techbull/nd04/nd04 mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

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FILE BIOSIS

FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 31 August 2005 (20050831/ED)

FILE RELOADED: 19 October 2003.

FILE EMBASE

FILE COVERS 1974 TO 25 Aug 2005 (20050825/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

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| | ENTRY | SESSION |
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Scientific and Technical Information Center

SEARCH REQUEST FORM

| Location (Bldg/Room#): 4A45 | e Number: 2- ه ا | Examiner # : 7414 Serial Number: 10 Results Format Preferred (ci | 1517,874 | |
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| To ensure an efficient and quality search | , please attach a copy of the co | | - I | |
| Title of Invention: | ciem fall | t of whole | derived Status | |
| Inventors (please provide full names) | | | | |
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| Earliest Priority Date: 6/13/ | 62 371 | of PCT/EPO3/ | 06175 6/12/03 | |
| Search Topic: Please provide a detailed statement of the elected species or structures, keywords, syn Define any terms that may have a special to the statement of the statemen | search topic, and describe as sp nonyms, acronyms, and registry | numbers, and combine with the con | cept or utility of the invention. | |
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